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RENAL CANCER ASSOCIATED WITH RENAL STONE.*

By John R. Coryell, M. D.,
Mayo Clinic, Rochester, Minn.

The object of this paper is not to advance a new theory nor to discredit an old one, but to record the macroscopic and microscopic findings in kidneys, the seat of both stone and cancer.

The method of procedure has been as follows:

1. Review of the primary pathologic diagnosis which was made on frozen sections stained with Unna's polychrome methylen blue in the diagnostic laboratory immediately after removal of the organ.

2. Study of the gross specimen.

3. Microscopic examination of sections from cortex, medulla and pelvis of specimens kept in 10 per cent formalin, frozen and stained with hematoxylin and eosin; also of serial paraffin sections of many specimens stained with Sudan III and Scharlacher, and with Weigert and Van Gieson.

The study covers all cases of renal cancer and renal stone from which tissue was removed in the Mayo Clinic from January 1, 1905, to July 1, 1914, a total of 145 cases, of which 131 were of stone only, 5 of cancer only, and 9 of cancer associated with stone.

* Submitted for publication, November 6, 1914.

Chronic Irritation from Renal Stone.

A great deal has been written on the relation between chronic irritation and the formation of cancer. That the two processes are frequently associated cannot be questioned. Whether cancer is the direct result of chronic irritation, or whether the latter plays the part of an extraneous exciting agent and determines the localization of the former in an organism which contains some sort of a chemical sensitizing substance (Loeb), or is influenced by some hereditary factor (Slye), is still an open question.

The expression, chronic irritation, is very broad in its scope and includes, under a single term, conditions induced by mechanical agents, as trauma, pressure (continuous or intermittent), friction, shock, dust, smoke, and foreign bodies of every kind as well as organisms living or dead; chemical agents, notably those concerned in the so-called occupational cancers of dye- and paraffin-workers and of chimney-sweeps; and physical agents, as heat, X-rays, light, electricity.

In 1823, Breschet and Ferrus stated their opinion that cancer invariably succeeded irritation or inflammation, and was

incapable of being developed except in places where one or other of those states had pre-existed (Walshe).

Virchow, in the early sixties of the last century, sought to explain the inception and development of cancer by irritation starting the cells upon a career of lawless growth. To-day Virchow's theory is accepted by many investigators as an explanation—to a certain degree—of the etiology of malignant proliferation.

Trauma, as a form of irritation, has been observed by Coley, who in 1911 reported personal observations on 250 cases of carcinoma, in which there was a history of trauma in 32.8 per cent. He refers to the work of Röpke who, in 1905, in a study of the material at the Surgical Clinic of Jena, collected statistics of 800 carcinomas "plus a larger number of cancers associated with chronic irritation," showing that in carcinoma chronic irritation seems to play the more important rôle. Ziegler states that of 170 cases of carcinoma, 37 of the patients, or 22 per cent, gave a history of a single antecedent trauma: Estlander gives 59 cases with 15 antecedent traumas (25.4 per cent); Snow 22 per cent in 143 cases; Henry 16.8 per cent in 196 cases—all preceded by a single trauma.

Levin, in 1910, published a table of 2882 cases of cancer involving different parts of the body. In 545, or 19.2 per cent, there was a definite history of previous local reaction.

The following are the principal reported examples of cancer developing at the site of irritation of varying duration and intensity:

Cancer of the uterus in women who have borne children, more common than in virgins.

Cancer of the cheek associated with the eating of very hot rice in certain provinces of China.

Cancer of the abdomen subsequent to burns from the Kangri or charcoal stove worn by the people of Kashmir.

Epithelioma of the mucous membrane of the mouth associated with chewing betel-nut mixed with lime—which is very irritating—by Hindoos.

Cancer of the penis developing on a chronic balanitis or unrelieved phimosis.

Gastric cancer developing on gastric ulcer (Wilson and MacCarty). "Hauser was the first to show that in gastric ulcer new tubular glands are formed, which are lined by cylindrical cells and may undergo cystic dilatation; and to call attention to the development of gastric cancer on a gastric ulcer" (Wilson). The most recent compilation of statistics from operative material shows that approximately 57.4 per cent of the gastric carcinomas develop on a gastric ulcer (Wilson and McDowell). Moynihan gives 60 per cent; Mayo Robson 59 per cent.

In an examination of 5000 appendices in the Mayo Clinic, 22 were found to have developed cancer. "Obliteration of lumen occurred in 22.8 per cent, and 90 per cent of the carcinomas occurred in partially or completely obliterated appendices. All were associated with chronic inflammation" (MacCarty and McGrath).

Of 27 colons with diverticulitis, 11 had cancer engrafted on them (Telling, quoted by Giffin and Wilson).

Cancer of gall-bladders previously affected with gall-stones. "In nearly all of the cases of our own series, gall-stones were present" (Mayo).

Cancer of the lip in smokers.

Tumors of the bladder, benign and malignant, in aniline dye-workers.

Cancer among X-ray workers.

Cancer of the breast after chronic mastitis.

Epithelioma after lupus or tuberculosis of the skin (L. Savatard).

Sarcomatoid hyperplasia of lymph nodes in tuberculosis.

Hypernephromas preceded by renal calculi (Ewing).

Cancer of the scrotum in chimney-sweeps and in paraffin workers.

Epitheliomas of the eye-lids. Fisher reports that of 88 cases, 46 per cent were in the lower lid and 36 per cent at the inner canthus. "These parts are usually hyperemic when the upper lid and outer canthus show comparatively little evidence of irritation. They are more frequently irritated by tears and foreign matter."

Rodent ulcer succeeding a hard pimple near the angle of the eye (Hutchinson).

Cancer on the margin of the lower lip, developing from a "crust."

Cancer from warts, cutaneous horns, sebaceous cysts, papillomas and ulcers (simple or specific) of the skin.

Cancer of the skin developing in tar, carbon and asphalt workers.

Prostatic cancer beginning where a chronic prostatitis is present (Young).

Local trauma of any kind (Coley).

Epitheliomas developing at the base of the right horn of cattle used to haul carts by a rope fastened to the right horn.

Cancer in horses where the bit irritates the corners of the mouth (Plicque).

Subcutaneous fibromas under the collar and girth of horses (Plicque).

Carcinoma of the posterior mammæ of dogs, the ones most frequently congested (Plicque).

Cancer of the upper lip of cats, the one more likely to be wounded.

Papillary epitheliomas on the tongues of rats fed for a long time on oats (Stahr).

Ribbert obtained small but typical papillary growths on the inner surface of the rabbit's lip by repeatedly scraping certain parts, again denuding them as soon as the epithelium was regenerated and finally allowing them to heal.

Clunet produced sarcoma in the rat by repeatedly exposing it to X-rays.

Rous has shown that more rapidly growing tumors developed at the site of a trauma than elsewhere in the body.

Kelley refers to papillomas developing on sheep's noses from grazing upon short stubble.

Perhaps the first to call attention to the pre-cancerous condition of the cell was Hutchinson, who spoke of it 50 years ago (Wood). Ribbert, in 1901, emphasized the importance of this stage of the cell.

Levin succeeded in increasing the susceptibility of rats to sarcoma by previous local irritation from injections of scarlet red and ether and established "the first experimental proof of the existence of a local 'pre-cancerous stage.'"

In kidneys, which are the seat of stones, one of the earliest changes is a proliferation of fibroblasts beneath the tubular epithelium. The new tissue thus produced apparently causes an upset of the balance between the epithelium and the connective tissue, which is followed by a proliferation of the epithelium. Here, at least, the epithelial multiplication seems to be due to a chronic irritation, set up by the stone. Thiersch accepts the pathologic condition in the connective tissue as causing it to become less resistant against the epithelial cells. "The epithelial growth follows the analogy of normal gland formation; while, owing to a process of adaptation to the abnormal environment and loss of function, the atypical structure of cancer results" (Ewing). Ewing refers to Hansemann, who uses the term "anaplasia" in conditions of tumor-cell changes which show unequal, asymmetrical and multipolar mitoses and destruction of chromosomes of frequent occurrence, particularly in the more malignant tumors. More or less anaplastic cells occur in inflammatory processes—cells with irregular mitoses. This strengthens the theory of the relationship between chronic irritation and tumor formation. Further, gametoid mitosis has been brought about in plants by means of chemical irritants, which would seem to add even more evidence to this theory.

In some of the sections of kidneys from cases of renal stone associated with renal cancer, there seems to be a tendency on the part of the cancer cells to mimic the renal tubules. In places, the epithelial cells supported by a delicate framework of connective tissue are arranged in columns, the central cells of which have apparently undergone degeneration and absorption, thus giving an appearance somewhat similar to that of renal tubules. The tubules are obviously of neoplastic origin; the component cells are distinctly cancerous and the general and minute appearance is different from that of regenerating tubules (Fig. 1). In this case the cancer was limited to and derived from the renal pelvis.

In several sections of kidneys containing stones are seen regenerating tubules. Their appearance, with both the low and high power, is embryonic. The newly formed or regenerating tubules are often surrounded by a small amount of delicate strands of connective tissue, supporting capillaries and at times slightly infiltrated with lymphoid cells. These tubules are somewhat narrower than the mature ones. The lining cells are proportionately larger than those of the epithelial lining of fully developed tubules. The nucleus is large and stains readily with hematoxylin; and at times nucleoli may be seen. The nuclear and cell membranes are distinct. Some cells contain two nuclei, but no chromosomes or early mitotic figures are seen (Fig. 2).

In kidneys, the seat of stone and cancer, where the cancer is not actually invading the substance of the gland, but where it is separated more or less completely by bands of connective tissue or by blood-vessels (Figs. 3 and 4), the preparatory inflammatory changes, *i. e.*, the formation of fibroblasts, new capillaries and lymphoid infiltration—which is often marked—seem to be entirely apart from the neoplasm. In other areas, where the inflammatory changes seem to be absent, or of a lesser degree, cells which are with great difficulty distinguished from neoplastic cells are present in varying numbers, interspersed among the connective-tissue cells. Whether these are embryonic connective-tissue cells or precursors of cancer cells it is almost, if not quite, impossible to decide. "Inflammatory hyperplasia passes by insensible gradations into a neoplastic growth" (Ewing). In places, at the periphery of the cancer, there is a network of fine connective tissue and in some places engorged capillaries. In the meshwork of connective tissue, as a rule, lymphoid cells predominate, but in many places there are cells which, although probably inflammatory in character, are with difficulty assigned to the group of neoplastic cells or to that of inflammatory ones. Their protoplasm stains with varying degrees of intensity with eosin; at times it is finely granular, at others it is clear and sometimes vacuolated. The nucleus usually stains deeply with hematoxylin, showing a well-defined border and a nucleolus. The cell outline is usually distinct. The shape of the cell is frequently modified by pressure—one often sees round, polygonal, fusiform and even flattened cells. When pressure is absent, the cell is usually round. In size, the cells vary somewhat, but are usually about 15 microns in diameter. In other words, in the same section one may see cells which are normal, others which are inflammatory, and still others which, apparently as a result of prolonged irritation, are distinctly neoplastic in character. If there is a line of demarcation between certain stages, or phases, of a chronic inflammatory process and neoplastic formation, it is, at times, very indistinct and it is difficult, if not impossible, to say where normal evolution stops and neoplasm begins (Fig. 5). Or, in other words, the stages of development of a cell under the influence of, or as a result of, an irritation, which is constant and prolonged, seem to be (1) normal, (2) inflammatory, (3) hyperplastic, or (4) neoplastic (either benign or malignant).

In all of the cases studied one may see destruction of the kidney, varying in degree from an involvement of a small portion in some to that of the entire organ in others. In those in which some of the parenchyma is left, there may be seen an interstitial and a parenchymatous nephritis; and in some of the specimens are seen areas of lymphoid infiltration, the central parts of which have undergone necrosis. In other areas are polymorphonuclear leucocytes, denoting abscess formation. Interstitial changes vary from 1 to 4 on a scale of 4, parenchymatous from 1 to 3 on a scale of 4 (Fig. 6). In kidneys, the seat of stones, in many places the epithelial cells lining the tubules show different stages of degeneration, having lost their vigor. There is frequently seen hyperplasia of the connective tissue, and the epithelium may have undergone (1) necrosis, (2) cyst formation and, in some specimens, (3) malignant metamorphosis. Notwithstanding the work of Kleinschmidt, who says, "Inflammatory changes of the kidney or pelvis of the kidney are not found in my cases," in

every case examined, 140 in all, not only in cases of renal stone associated with cancer, but also in kidneys containing only stones, inflammatory changes are seen. They were found in the parenchyma in some cases, in others the process was limited to the pelvis, and in still others both were involved. The type of inflammatory reaction varied from that of an acute process in some to a well-marked chronic type in others (Fig. 7).

In several specimens the tubules are dilated in varying degrees, some being 4 or 5 times their normal size, and cysts are seen, but not frequently.

Stone-pockets are very commonly observed. Some are microscopic in size. Other kidneys consist entirely of connective-tissue stone-pockets (Fig. 8). The walls of the stone-pockets are made up of connective-tissue stroma with lymphoid infiltration lined with 2 or 3 layers of cuboidal, or, in some places, flat cells.

Varying amounts of fat are not infrequently found in the pelvis of kidneys containing stones. Braasch has called attention to this fact. Smooth muscle fibers are not infrequently seen in the parenchyma of kidneys containing stones. In several specimens of this series may be seen spindle cells with long nuclei, the protoplasm of which is usually granular and stains readily with eosin. Some of the nuclei are oval, others are very long and rod-shaped. These obviously belong to smooth muscle fiber. An explanation of the occurrence of the smooth muscle fibers is found in the fact that in fœtal life the kidney is very rich in smooth muscle, whereas in adult life it is found only in the capsule and wall of the pelvis. The collecting tubules, derived from the Wolffian duct, are surrounded by smooth muscle fibers in early fœtal life. These fibers disappear as development advances. At times, this disappearance may be incomplete and small rudiments of smooth muscle fiber may occasionally remain in the pyramids (Nicholson). In some of the sections studied, these fibers are also seen in the medulla and cortex. Nicholson says that the muscle comes from the layer of cells which also forms the renal epithelium. This, as shown by Huber, is the mesoblast. Areas in which development has been arrested at an early period may contain the mother-cell of the epithelium and of the plain muscle.

In squamous epitheliomas arising from the pelvis, of which there are five definite cases in this series, the origin of the neoplasm is probably from the epithelium of the renal pelvis (Figs. 9 and 10). The renal pelvis is derived embryologically from the Wolffian duct, which is derived, in part at least, from the epiblast. Epiblast almost always gives rise to squamous epithelium; therefore, it is at least possible that squamous epitheliomas are developed from the epithelium of the renal pelvis. Stoerck says that tumors starting in the renal pelvis are usually associated with conditions of chronic irritation, as, for example, from stones.

In one case of cancer associated with stones the neoplasm started in the epithelium lining the tubules. In this particular case it was not ascertained at which part of the tubule the cancer took its origin, but from the glomeruli to the end of the collecting tubules the lining epithelium had undergone various degrees of degeneration and in different places along the tubule hyperplasia of the epithelium was seen. In one case (Fig. 11) the tubular "offshoot" was malignant. Thus we see that cancer of the kidney which contains stone may arise from the tubules. In some of these cases, colloid degeneration is seen (Fig. 12). At times the stones are limited to the parenchyma (Fig. 13). Here the stones are shown in the tubules. There were none in the renal pelvis in this case.

The origin and character of a cell, not infrequently found in kidneys affected with stones, and which occurred in 28 cases in a series of 140, has been somewhat difficult to determine. In some specimens it was not commonly seen; in others it was of very frequent occurrence and was even found in groups in several specimens. It was a large refractile cell, about 20 to 30 microns in diameter. The cell membrane was usually distinct, but at times invisible. With the hematoxylin and eosin stain, the protoplasm was very pale, practically white or at most a pale pink, occasionally clear but usually granular, and some of the cells contained vacuoles. The nucleus, not always present and at times fragmented, was usually about 3 to 4 microns in diameter. It stained with a varying degree of intensity, at times quite deeply. Its border was usually well defined. No mitoses were seen in these cells. In general arrangement, these cells frequently gave an appearance somewhat resembling that of a mesothelioma (so-called hypernephroma). They were often arranged in columns along fine strands of connective tissue, which, at times, supported engorged capillaries (Fig. 14). The engorged capillaries, however, were of infrequent occurrence. In many specimens lymphoid cells were seen, varying in number from a few cells to a marked infiltration, among the clear cells. Fibroblasts were also seen scattered among the delicate strands of connective tissue. In some of the sections were red blood cells interspersed among the clear cells. In some places these groups of cells were surrounded by well-defined bands of connective tissue; in others, a few of the clear cells were found scattered between the renal tubules. Several sections showed cells somewhat similar to these, but they were found in infarcts; were apparently derived from connective-tissue cells and were probably largely hydropic in character, since they contained very little fat. From the large, deeply-staining nucleus, distinct nuclear and cell membranes, and the fact that the protoplasm was light in many cells, it was presumed that the cells just described were embryonic in character.

Zebbe describes similar cells and says they may arise from connective tissue, endothelium or from phagocytes; that they are found in large white and contracted kidneys, but not in acute nephritis nor in diabetics; that they are similar to cells found in the lung and thyroid and Grawitzian tumors (mesotheliomas); and that they are peculiar to the kidney under certain conditions.

Fig. 15 shows this cell in an early stage of development. Here it seems to be in a renal tubule, in which all of the cells are of the same type. They contain granules which stain with fat stains, as do the cells from other cases which are more

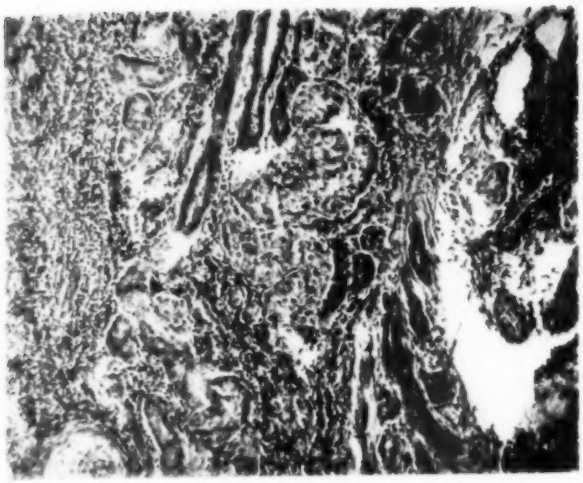

FIG. 1 (A2662). × 120. Attempt of cancer cells to mimic renal tubules in their arrangement.

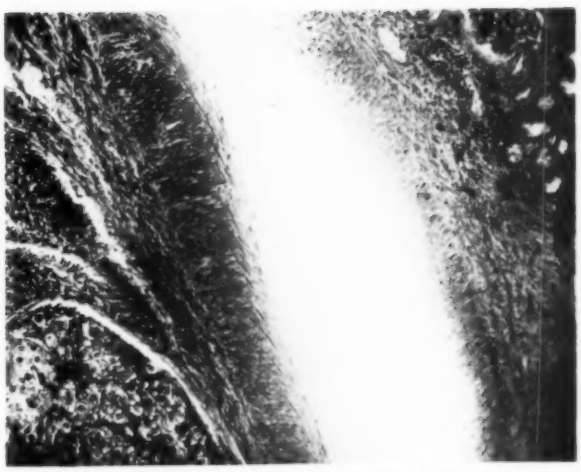

FIG. 3 (A49100). × 50. Renal substance (glomeruli and tubules) with a large artery separating it from a cancerous area.

FIG. 2 (A91687). × 250. Regenerating renal tubules, showing embryonic character of the cells. Large, deeply-stained nuclei in lower right corner. Above are old tubules, cut longitudinally, showing disintegrating cells.

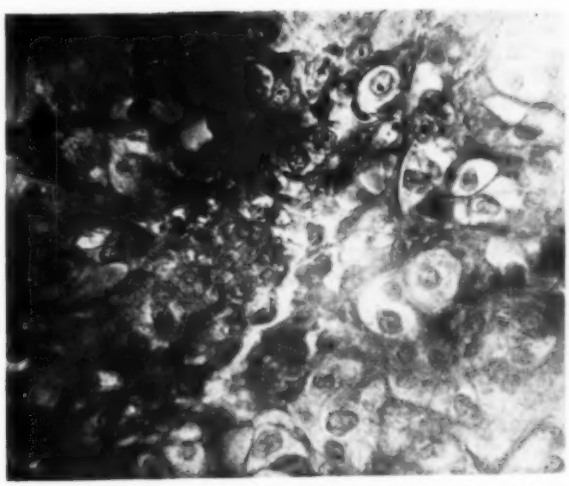

FIG. 4 (A49100). × 250. Cancerous area shown in Fig. 3. Large polyhedral cells, 20 microns in diameter; pale-staining, slightly eccentric nuclei; very little intercellular substance.

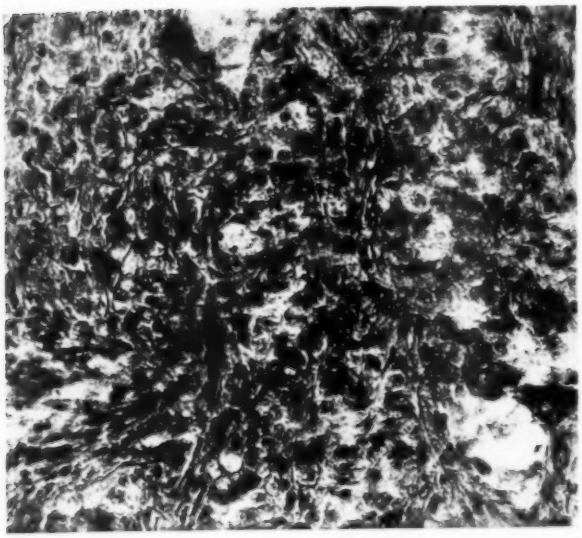

FIG. 5 (A75691). × 250. Section through area of inflammatory and neoplastic cells. Tubules very small and greatly diminished in number. The lining cells spherical, with large deeply-stained nuclei; scanty protoplasm, surrounded by well-defined strands of connective tissue with oval nuclei. At other times, they are disposed irregularly. Cancer cells at times mimic the renal tubules in their arrangement of cells supported by delicate threads of connective tissue. The cells are polygonal; protoplasm very finely granular; limiting membrane distinct.

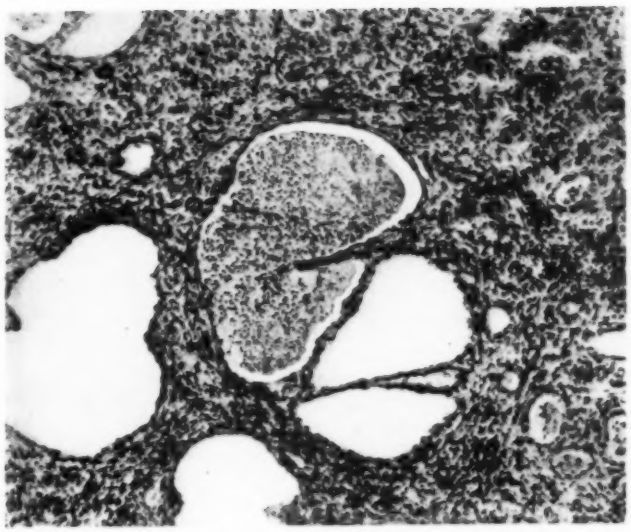

FIG. 7 (A73915). × 120. Section of kidney. Dilated tubules contain pus, polymorphonuclears and debris. Walls of connective tissue with 1 to 3 layers of cuboidal cells whose nuclei are deeply stained; very little protoplasm.

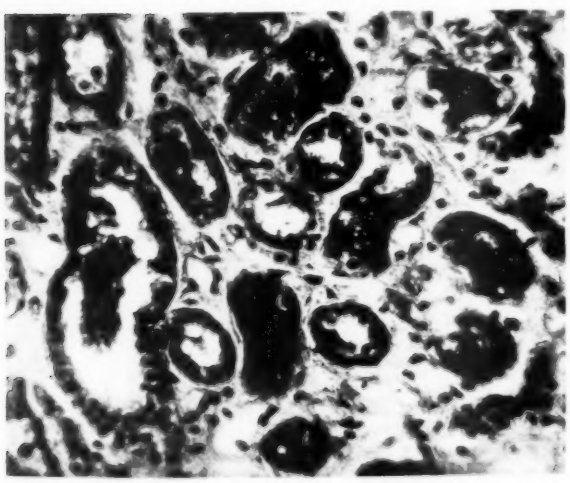

FIG. 6 (A75806). × 50. Through an area of cut-off degenerating renal tubules. Shows disintegrating cells lining the tubules; nuclei indistinct. Protoplasm granular; marked increase in connective tissue.

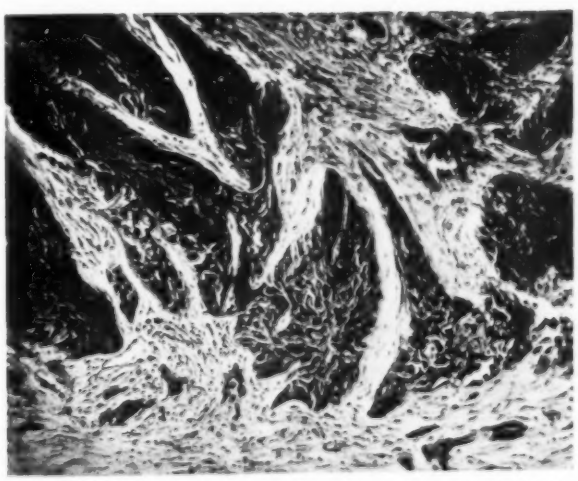

FIG. 9 (A38096). × 100. Section through squamous-celled carcinoma of renal pelvis. Shows arrangement of cancer cells and connective tissue.

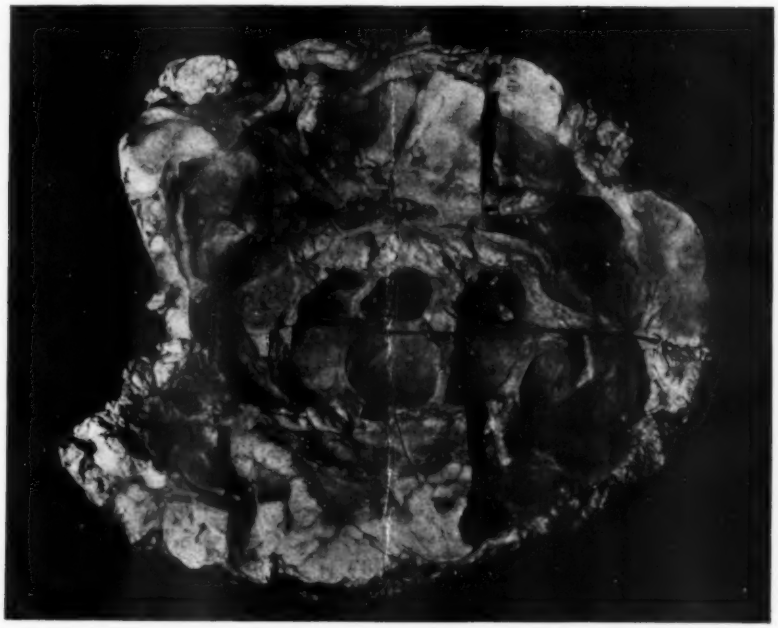

FIG. 8 (82907). Left kidney one-third normal size. Fat and fibrous tissue throughout. Stones and stone-pockets throughout.

FIG. 10 (A23253). × 250. Squamous-celled cancer with hyaline degeneration.

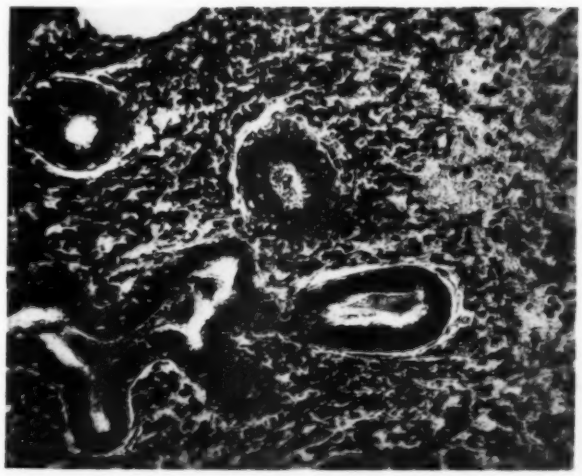

FIG. 11 (A74679). Cancer originating in the tubules; chronic parenchymatous nephritis (2); chronic interstitial nephritis (2); suppurative nephritis 1. 150 D. mag. of area showing branching cancer tubules, the lining cells of which appear to be invading the stroma. It also shows lymphoid infiltration.

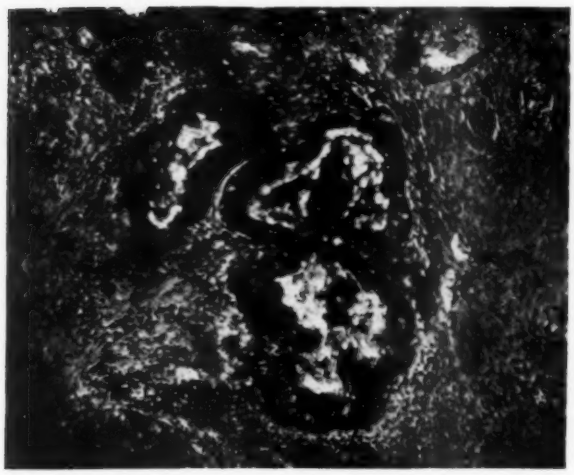

FIG. 12 (A91370). ×150. Section of papillary adenomatous type of cancer with cells forming acini filled with colloid substance. The cells are supported by delicate strands of connective tissue: the latter sends in strands which, covered with cells, give a papillary appearance. Lymphoid cells are scattered between the acini.

FIG. 14 (A69689). ×250. Section through area of "fat-hydropic" cells arranged in columns, suggesting a mesothelioma. Cells supported by strands of connective tissue, in which are seen lymphoid cells.

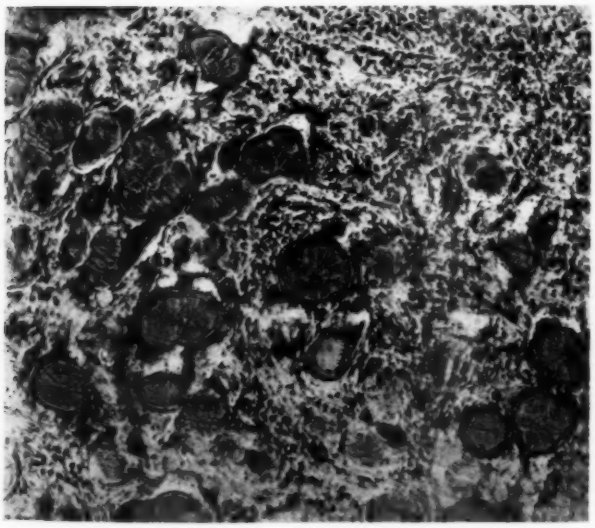

FIG. 13 (A86712). ×120. Section through tubules containing stones. Tubules lined with flattened cells, 1 to 2 layers. Stroma increased; lymphoid infiltration. Stones dark brown in color; concentric lamellæ; radial striations.

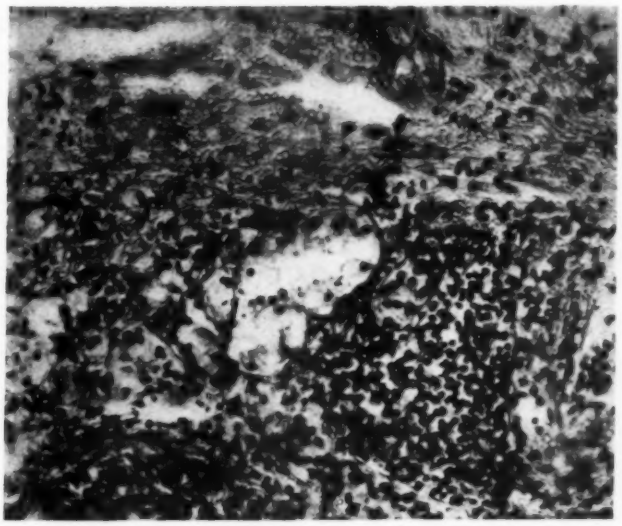

FIG. 15 (75542). ×250. Early stage of "fat-hydropic" cells seen in the renal tubules (fat stain).

advanced (Fig. 14), and are arranged in masses or columns. They are not found in normal adrenals, but are similar to cells found in mesotheliomas. They are found in the kidney, are of renal origin and appear to come from the renal tubules. They are found in kidneys containing stones and also in kidneys containing stones and cancer.

TABULATED SUMMARY OF CASES OF RENAL CANCER ASSOCIATED WITH RENAL STONE REPORTED IN THE LITERATURE.

Author.	Number of Cases.	Cancer.	Stone.
Ransohoff.	1	Duration 12 mos.	Duration much longer.
Noble and Babcock.	1?	Papillary, in pelvis.	
Albarran and Imbert.	Collected 23, 3 personal.	All in adults.	
Nicholich.	1	Papillary, in pelvis.	Several.
Minet.	3	Papillary, in pelvis.	Multiple.
Oraison and Nodal.	2		
Porter.	1		53 yrs. history. Wt. 1920 gr'ns
Deaver.	1	Ureter.	Ureter.
Rafin.	3	1. Epithelioma. 2. Mesothelioma. 3. ?	
Lacassagne.	1	Pelvis.	

In reporting the foregoing cases, the authors dwelt largely on the clinical problems and very little on the pathologic aspects. It is at once seen that cancer associated with stone in the kidney is not of common occurrence, 3 being the largest number of cases hitherto reported by any one author. Albarran and Imbert collected and reported 26 in two or three hundred cases of renal tumors.

In the Mayo Clinic, since April 5, 1905, that is, in 9 years and 6 months, there have been removed 140 kidneys containing stones, and of these, 9 also contained cancer, or about 6.5 per cent. During the same period, 6 nephrectomies were done for cancer of the kidney, one of which was metastatic. The proportion, therefore, is 9 cancers of the kidney associated with stones to 5 cancers without stones, or 64+ per cent for the former and 35+ per cent for the latter. This is about the same as in gastric cancer developing on a gastric ulcer and of other cancers developing at the site of chronic irritation.

Tuberculosis was found in only one of the 140 kidneys containing stones.

Amyloid degeneration was found in four cases.

Polycystic kidney was found in one case.

The equilibrium or mutual counteraction between remission of cell multiplication and indefinite reproduction is very sensitive; and until this is better understood, the nature, development and treatment of cancer will remain an enigma. Until the origin and development of cancer has been assigned to some definite cause, individuals will continue to accept or to reject theories according to their own ideas. Certainly some are improbable, while, on the other hand, some have all the appearance of probability and seem almost certainly true. From the above study, therefore, it has seemed useless even to attempt a consideration of the relative merits of the different hypotheses. However, from a clinical and more particularly from a pathologic study, one must admit that irritation is a strong etiologic factor in the development of renal cancer.

SUMMARY.

1. Renal epithelium (tubular and pelvic) not infrequently regenerates.

2. Renal tubules regenerate not infrequently as a whole.

3. The stages of development of renal epithelium under the influence of or as a result of irritation which is constant and prolonged are (1) normal, (2) inflammatory, (3) hyperplastic, (4) neoplastic (which may be either benign or malignant). In the kidney there seems to be no distinct line of demarcation between certain stages or phases of a chronic-inflammatory process and neoplastic formation, and it is impossible to say where normal processes cease and neoplastic processes begin.

4. The preparatory phenomena of renal new-growth seem to take place not in the area actually irritated, *i. e.*, not in the area which shows actual inflammatory reaction, but just beyond the same.

5. Even if heredity plays the same rôle in human cancer as it seems to play in mouse cancer, chronic irritation in the kidney is still of very great importance, in that it determines the location of the neoplasm.

6. There is, at times, an attempt on the part of the neoplasm to mimic the structure of the kidney by a columnar arrangement of cells and the formation of a lumen.

7. Renal cancer develops from the epithelium, both of the pelvis and of the tubules.

8. In all specimens studied, the kidney in some portion showed an inflammatory reaction. The destruction of the renal substance varied in degree and was brought about by interstitial or parenchymatous changes or both; and suppuration was of frequent occurrence.

9. The epithelial lining of renal tubules may, under the influence of renal stone, (1) necrose, (2) form cysts, or (3) become malignant.

10. After having seen the gradual changes from normal tissue to inflammatory, from inflammatory to hyperplastic, and from hyperplastic to neoplastic, it appears probable that the chronic irritation brought on by the stones was the direct cause of the cancer.

11. In all the cases of renal cancer associated with renal stone, a large, light, fat-containing cell is found, sometimes singly, sometimes arranged in groups, and sometimes in definite columns. It has its origin in the tubules of the kidney. Further study will be made of this cell.

12. Of the total number of kidneys with cancer removed at the Mayo Clinic, 64+ per cent were associated with stones and 35+ per cent were without stones.

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AN EXPERIMENTAL STUDY OF LAVAGE IN ACUTE CARBOLIC ACID POISONING.*

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Acute poisoning with phenol, or carbolic acid, is one of the commonest forms of fatal poisoning met with in this country and, according to Blyth,[1] in England it occupies the highest place in the fatality list of all poisons.

Although phenol poisoning is now fortunately but rarely met with in surgical practice, the drug is still a favorite one among those who are bent on self-destruction and is often, also, swallowed accidentally for other medicines. Owing to its rapidly toxic action upon the central nervous system and the heart, phenol is one of the most quickly fatal poisons, and almost every medical man of experience has seen or heard of a man or a woman succumbing rapidly in some thirty minutes, sometimes less, after swallowing an ounce of pure carbolic acid. To save a patient, therefore, very prompt attention is required, and appropriate first aid is of vital importance.

Lavage of the stomach has for a long time been recommended in all cases of phenol poisoning, and for this purpose either plain water or watery solutions of various substances have been employed. Numerous substances—albumen, syrup of lime, solutions of iodine or potassium permanganate, milk, and others—have been recommended for this purpose. Two drugs, however, in particular, have been used in this connection on seemingly rational grounds. These are alcohol and sodium sulphate.

The internal use of alcohol in carbolic-acid poisoning originated from a rather naive and, as we shall see later, fallacious deduction that, because alcohol is an excellent antidote for carbolic-acid burns of the skin, therefore it must be useful in the treatment of carbolic-acid burns of the stomach. This use of alcohol as an antidote in phenol poisoning was first brought before the medical profession by a certain Dr. Seneca D. Powell, of New York City, who was in the habit of demonstrating his theory by washing his hands in pure carbolic acid and then in alcohol, and even filling his mouth with pure acid and quickly rinsing it with 95 per cent alcohol without experiencing harmful results. From these experiments he drew the general conclusion that alcohol is an antidote to carbolic acid and suggested its internal use in cases of poisoning.[2] The first such use of alcohol in poisoning cases on record is

* Read before The Johns Hopkins Hospital Medical Society, Nov. 16, 1914.

credited to Dr. J. D. Buchanan, who washed the stomach of a patient, who had taken one ounce of the acid, with two quarts of 95 per cent alcohol.[3] Since then a number of isolated cases thus treated are to be found in the literature, from which the most positive conclusions have been drawn. Thus, for example, Kelly[4] in 1899, after reporting one successful case, remarks that "alcohol is undoubtedly the best antidote for all cases of carbolic acid poisoning, and, indeed, is an absolute antidote." Phelps[5] states: "In cases of carbolic-acid poisoning, if immediately after the administration of the poison alcohol be thrown into the stomach the poisonous effects of the carbolic acid will be neutralized." Again, Pinkney,[6] after relating a fatal case, says: "The amount of carbolic acid left in the stomach and intestines when alcohol came in contact with it was rendered harmless, and the general action of the slowly absorbed poison was checked immediately."

The only really scientific attempt to determine the value of alcohol in this connection was made in 1906 by Clarke and Brown.[7] These authors collected and analyzed all the clinical cases available which had been treated with alcohol, and also made some experiments on animals. Their conclusions are, however, somewhat contradictory. On the one hand, from a study of the clinical cases, they conclude "there was no material difference in the mortality whether the stomach was washed with alcohol or with some other liquid, and the apparently greater constitutional symptoms when the drug was taken with alcohol than when taken clear or in water seemed to throw grave doubts on the antidotal power of alcohol." On the other hand, after their experimental work they conclude: "In cases of poisoning, lavage with alcohol is apparently an effective method of treatment," and "the procedure recommended is immediate abundant lavage with 10 per cent alcohol, followed by lavage with plain water, and stimulation as indicated."

It will thus be seen that the value of alcohol in carbolic-acid poisoning is still unsettled.

A very similar confusion as to its usefulness prevails regarding sodium sulphate. The introduction of this drug in the treatment of phenol poisoning goes back to the observations of Baumann in 1876.[8] Baumann painted the skin of a dog with phenol and at the same time fed the animal on sodium sulphate, and found paired sulphates in the urine. He, therefore, recommended the sulphates as direct chemical antidotes to carbolic acid. Cerna[9] and Cafrawy[10] each made experiments on animals, their observations apparently confirming this view, but their work is not regarded as convincing, as the doses of carbolic acid which they used were too small. Clinically, Sonenburg[11] found that the dark color of the urine and other symptoms rapidly disappeared after the administration of sodium sulphate. On the other hand, Küster[12] found that intravenous injections of sodium sulphate had little or no effect on phenol poisoning; and Tauber's careful work[13] threw still more doubt upon the subject. The latter observer studied the effect of subcutaneous and intravenous injections of sodium sulphate, pyrosulphate, ethylsulphate, sulphite, dithionate, and thiosulphate, in animals poisoned with carbolic acid, and noted a neutralization or detoxification of the phenol only in the case of the sodium sulphite, from which it would seem that phenol does not combine with the sulphates as such in the body, but with organic sulphur compounds, which are in process of being oxidized to sulphuric acid, as illustrated by the following formula:

$$\underset{\text{phenol}}{C_6H_5OH} + \underset{\substack{\text{acid sodium}\\ \text{sulphite}}}{HSO_3Na} + O = \underset{\substack{\text{sodium phenol}\\ \text{sulphonate}}}{C_6H_5OSO_3Na} + H_2O.$$

The use of the sulphite intravenously would hardly be suitable in clinical cases, nor would its employment even *per os* be devoid of danger. Sodium sulphate, however, has been employed in lavage, and various authors have reported recoveries after its administration. As an instance may be cited the case of Model.[14] A girl 9 years of age had swallowed a tablespoonful of carbolic acid on an empty stomach, and quickly became unconscious. Two hours later her stomach was washed out with a strong solution of Glauber's salts, and she recovered.

The present research was undertaken with the object of ascertaining the comparative advantages of various modes of lavage in phenol poisoning, and thus determining the most suitable and efficient method of rendering first aid in these unfortunate cases. Such a study was deemed particularly desirable for two reasons: firstly, because of the confusion and lack of agreement among various writers on the subject; and, secondly, because through the experimental work of Sollmann, Hanzlik and Pilcher[15] we have good reason to believe that lavage in these cases may really be of some benefit and not a hopeless procedure. These observers made quantitative studies on the gastro-intestinal absorption of drugs and found that "When phenol is placed in the alimentary canal the absorption is at first very rapid, but is quickly checked and soon practically arrested"; and "When phenol is placed in the stomach, only traces pass into the intestine; a large proportion could be removed by gastric lavage, even several hours after the phenol was taken."

I have introduced liquefied carbolic acid, both in concentrated solution and in various dilutions, through a stomach tube into the stomachs of various animals, and washed their stomachs out thoroughly at different periods of time after the appearance of the toxic symptoms. As is well known, the first symptoms of carbolic-acid poisoning in higher animals are weakness and a peculiar muscular tremor different from that produced by other convulsants, such as physostigmin and santonin[16]; these are quickly followed by clonic convulsions, collapse, coma and death. The animal suffers very little pain. In our experiments the animals were first anesthetized with ether, but as phenol, in the doses used, itself quickly paralyzes the central nervous system and the animals never show signs of pain, this preliminary anesthesia, for closer scientific observation, was dispensed with in some of the later experiments. This anesthetic action of carbolic acid is well known, and has also been confirmed in man. In the

human being convulsions are comparatively rarely seen, and when large quantities have been taken almost immediate unconsciousness may result.

Animals Studied.

The animals most suitable for the study of lavage are cats and dogs. For further pharmacological analysis some experiments were made on frogs, rabbits, white mice and white rats. A large number of experiments were made. To give them all even in tabular form would require too much valuable space. Only a sufficient number of protocols is, therefore, given here to illustrate the salient features of the investigation.

For convenience of description the dosage of phenol in this paper is usually indicated in cubic centimeters of the official phenol liquefactum of the United States Pharmacopœia, or acidum carbolicum liquefactum of the British Pharmacopœia. Phenol, as is well known, consists of solid crystals, which readily take up 10 parts of water forming the liquid phenol. One cubic centimeter of this liquid is practically equivalent to 1 gram of phenol.

Substances Studied.

Solutions or suspensions of various substances were tried in washing out the phenol from the stomach. Among these were egg albumen, alcohol, sodium sulphate, sodium sulphite, and syrup of lime. Of these albumen was found of very little value and sodium sulphite was too poisonous to be taken internally. Lime water and syrup of lime have been recommended by some authors in the hope that an insoluble combination might be formed in the stomach, but our experience with them was very unsatisfactory. My chief attention was therefore directed to the comparative study of the three reagents most used in phenol poisoning, namely, plain water, and aqueous solutions of alcohol and of sodium sulphate.

Lethal Dose.

Before attempting to save the animals by lavage, it was necessary to determine the smallest dose of the drug required to kill the animal in a short time. As even small doses of phenol through continual convulsions and exhaustion will kill an animal in a prolonged period of time, our experiments were directed to determining the smallest lethal dose, causing acute exitus in an hour or two. In this respect, a marked difference was found between the dog and cat. Though the symptoms and signs of poisoning are the same in both kinds of animal, cats were found much more susceptible to carbolic acid. The lethal dose for dogs was found to be about 0.5 cc. of the official phenol liquefactum per kilo. of weight; that for cats less than 0.1 cc. per kilo. of weight. These figures agree very well with those of Tollens[17] and other experimenters. As might have been expected, the presence of food in the stomach retards the absorption and binds some of the drug, so that a larger dose is required and the symptoms of poisoning appear later. The folowing protocols will serve to illustrate the rapidly fatal toxicity of carbolic acid:

Exp. 3. Oct. 29, 1913. Cat. Wt. 2 kgs. Stomach empty. Has not been fed since day before.

Introduced into stomach through rubber tube 0.15 cc. of acidum carbolicum liquefactum, mixed with water to make a 10 per cent solution.

Clonic convulsions appeared in 2½ minutes and death, from stoppage of heart and respiration simultaneously, one minute later.

Exp. 34. July 30, 1914. Male dog. Wt. 13 kgs. Stomach empty.

10.20 a. m., introduced 6.5 cc. of pure carbolic acid mixed with water to make a 10 per cent solution. Clonic convulsions set in 2½ minutes later.

10.40 Dog died while being put on table for lavage.

Exp. 1. Oct. 13, 1913. Cat. Wt. 3 kgs.

Introduced through stomach tube 1 cc. of pure carbolic acid diluted one-half with water.

2 minutes later, general clonic convulsions of body and jaws.

20 minutes later, continued convulsions; pulse 130 per minute, fairly strong.

30 minutes later, breathing shallow and very slow; pulse weak, 120 per minute.

60 minutes later, convulsions and retching movements.

96 minutes later, continued convulsions, coma, and very weak pulse, 120 per minute.

110 minutes later, heart irregular and can hardly be heard with stethoscope.

2 hours later, still in convulsions; bloody vomitus.

2½ hours later, convulsions weaker.

5 hours later, dead.

At autopsy, lungs very markedly congested, heart dilated, and stomach *full of food*.

It may be interesting in this connection to note the fatal dose of carbolic acid in man. Very small doses of carbolic acid taken internally have resulted fatally. Thus in one case, a girl, 24 years old, died shortly after taking 1.5 gm. of phenol.[18] In another case one drachm (4 cc.) proved fatal to a girl of 17 years.[19] Ordinarily the fatal dose, however, is much higher. Lewin[20] places it at from 8.5 to 60 gm. This corresponds with the ordinary doses taken for suicidal purposes in this country, which average about one ounce. If we reckon the average weight of man at about 70 kgs. it will be seen that the lethal dose per kilo. for man approaches very closely to that for the dog.

Results of Lavage in Cats.

The success or failure of lavage in rescuing the animal was found to depend on the amount of phenol introduced, the time of lavage after the appearance of the toxic symptoms, and the solutions used.

In poisonings with small, though lethal, doses of carbolic acid, in which the stomach was washed immediately on the appearance of convulsions, that is, three to five minutes after ingestion of the drug, it was found that the animals could in most cases be saved by washing the stomach out thoroughly with either plain water or a concentrated solution of sodium sulphate. Lavage with solutions of alcohol was followed sometimes by recovery, but more often by death.

After larger doses of phenol *prompt* lavage with alcohol resulted almost invariably in death; washing the stomach with

plain water failed likewise to save the animal; but lavage with sodium sulphate was often attended with favorable results, and the animal either survived longer or completely recovered.

After *later* lavage, however, it was found that washing with alcohol or plain water was invariably followed by death, whereas lavage with sodium sulphate occasionally saved the animal. As cats are extremely susceptible to phenol poisoning, lavage could never be used to advantage later than 10 minutes after introduction of the poison into the system.

The following protocols will illustrate some of the above-mentioned results:

EXP. 2. Oct. 22, 1913. Cat. Wt. 2.5 kgs.

Introduced through stomach tube 0.5 cc. pure phenol liquefactum mixed with five times its volume of water. Stomach empty.

Convulsions appeared one minute later. Lavage with plain water 2 minutes later. Death in 5 minutes.

EXP. 12. Nov. 10, 1914. Cat. Wt. 3.2 kgs.

Introduced through stomach tube 3.2 cc. of 10 per cent carbolic acid solution. The animal had been fed a few hours previously. Convulsions began in 3 minutes.

Lavage with plain water one minute later. In 10 minutes the animal had recovered.

EXP. 6. Oct. 20, 1913. Cat. Wt. 1.5 kgs.

Introduced through stomach tube 1 cc. of pure carbolic acid mixed with an equal volume of water. The animal had been fed a short time previously.

Convulsions began in 2 minutes. Then immediate lavage was begun with 40 per cent alcohol followed by plain water. The animal died in 5 minutes.

EXP. 15. Nov. 12, 1914. Cat. Wt. 2.9 kgs.

Introduced through stomach tube 2.9 cc. of 10 per cent carbolic acid solution.

Convulsions began in 2½ minutes.

Lavage with 20 per cent alcohol 3 minutes later, then with water. Death occurred 5 minutes later through sudden stoppage of the heart.

EXP. 8. Oct. 12, 1913. Cat. Wt. 2.5 kgs.

Introduced 0.5 cc. of pure carbolic, acid diluted with 10 times its volume of water. The stomach contained no food.

Convulsions appeared in 3 minutes.

Began washing with concentrated solution of sodium sulphate one minute later.

At the end of 10 minutes the heart and respiration were good.

20 minutes after poisoning, the animal recovered consciousness and cried.

30 minutes after poisoning the convulsions subsided, only muscular tremor being noted.

1 hour and 15 minutes later the cat lay quietly, drank water, and was in good condition.

EXP. 17. Nov. 10, 1913. Cat. Wt. 2.5

Introduced through stomach tube 1.25 cc. of 10 per cent carbolic acid.

Convulsions appeared in 2 minutes. After 5 minutes, lavage with sodium sulphate.

Heart stopped suddenly.

RESULTS OF LAVAGE IN DOGS.

Our experience with dogs was more promising than with cats. Whereas the latter are extremely susceptible to the toxic action of phenol, dogs are able to withstand larger quantities of it and for a longer period of time. The results of the findings may be briefly summarized as follows:

By *immediate* lavage after introduction of lethal quantities of phenol it is possible to save the animals by washing, irrespective of the medium used, even though toxic symptoms are present.

After larger doses of the drug immediate lavage with sodium sulphate or with plain water may save the animal; washing with alcohol almost always results in death.

In *late* lavage (about 15 minutes after the introduction of the poison into the stomach) washing with sodium sulphate solution was found to give the best results; next in usefulness was plain water, whereas washing with alcohol resulted almost invariably fatally.

The following protocols will illustrate some of the findings:

EXP. 23. July 20, 1914. Dog. Wt. 5.4 kgs.

Introduced through stomach tube 5.4 cc. of pure carbolic acid mixed with 10 parts of water.

Clonic convulsions began in 3 minutes. Copious lavage with 2 litres of plain water was begun 2 minutes later and continued until the drug could not be smelled in the washings.

Taken off the table unconscious, but with heart and respiration in good condition. Recovery in 1 hour.

Here we see recovery after a large dose of phenol, following *immediate* lavage with water.

EXP. 30. July 30, 1914. Dog. Wt. 10.5 kgs.

10.10. Introduced through stomach tube 5.25 cc. of pure carbolic acid in 10 parts of water.

Clonic convulsions began in 2 minutes.

10.30 a. m. Began lavage with plain water, 3 litres.

11.15 a. m. Convulsions much less violent, but still unconscious.

2.00 p. m. Convulsions continue.

3.30 p. m. Still unconscious.

July 31, 9 a. m. Found dead.

Here we see that washing with water, begun 20 minutes after ingestion of the poison, was of no avail.

EXP. 20. July 22, 1914. Large dog. Wt. 11 kgs.

3.38 p. m. Introduced 11 cc. of pure carbolic acid mixed with 10 times its volume of water.

2.55 p. m. Dog shows a slight tremor, but no convulsions. No vomiting.

2.58 p. m. Introduced 11 cc. more of pure carbolic acid in 100 cc. of water.

3.20 p. m. Dog sick, lying down, half unconscious.

3.23 p. m. Began washing with concentrated solution of sodium sulphate. Some food was found in stomach.

3.34 p. m. Lavage stopped. Dog taken off table in good condition. Was found in perfect health next morning.

In this case recovery took place after lavage with sodium sulphate begun 45 minutes after the first dose of the poison, and after an enormous total quantity of carbolic acid, 22 cc. in all. The presence of food in the stomach undoubtedly favored the successful outcome.

EXP. 25. July 23, 1914. Dog. Wt. 6 kgs. In poor health. Suffering from distemper.

Introduced through stomach tube 3 cc. pure carbolic acid with 5 parts of water.

Convulsions began 3 minutes later; unconscious.

10 minutes later lavage with sodium sulphate solution. Recovery, but death a day later.

Here we find recovery, at least temporary, in a previously sick dog, after lavage with sodium sulphate solution.

Exp. 36. July, 1914. Dog. Wt. 7 kgs.
1.24 p. m. Gave 3.5 cc. pure carbolic acid in 10 parts of water.
1.25 p. m. Clonic convulsions.
1.40 p. m. Began washing with 15 per cent alcohol.
1.41 p. m. Dog died on the table. Further washing revealed food in the stomach.

Here we had sudden death while washing with alcohol, after a not excessive dose of phenol and with the stomach full of food. Compare this experiment with Exp. 20, described above.

Exp. 40. July, 1914. Dog. Wt. 7 kgs.
Introduced 7 cc. of pure carbolic acid mixed with 10 parts of water.
Clonic convulsions set in 2 minutes later.
Immediately after lavage was begun with 20 per cent alcohol, followed by plain water.
The respirations stopped suddenly and the heart beat became imperceptible.
Gave artificial respiration and massage of heart.
Animal began to breathe again 5 minutes later.
Taken off table in moribund condition.
Next day signs of recovery, but death later.

Analysis and Discussion.

From the above protocols it will be seen that introduction of phenol into the stomach of cats and dogs, in sufficient quantity will without a therapeutic procedure invariably produce death; but that the animal can often be saved by thorough lavage of the stomach. Of the three reagents used for this purpose and chiefly studied in this connection, sodium sulphate was found to be the most efficient, next in order being plain water. Alcohol was found to be distinctly deleterious, and often appeared to hasten a fatal issue. The chances of rescuing an animal depend firstly on the dose of poison swallowed or introduced into the stomach; secondly, on the promptness with which the lavage is begun, and, thirdly, on the solution used in washing the stomach. The earlier the lavage is begun the greater the chances of recovery, even though a large quantity of the poison has been taken. The presence of food in the stomach greatly increases the chances of recovery. In my experiments I have purposely refrained from any other measures in resuscitating the animal except artificial respiration, massaging the precordium, and keeping the animal warm; but the judicious use of stimulants would seem to be indicated, although in the few experiments in which I tried them no striking effects were noted. For the use of emetics recommended by some authors, there seems to be no rational ground.

If we compare the lethal dose of phenol per kilo. of a dog with the fatal dose given by most authors for man, we shall see that the toxicity of phenol for the two is about the same. We have reason, therefore, to expect that the same measures may be applicable in cases of carbolic-acid poisoning in the human being, and indeed, as already mentioned, some clinical reports of lavage with sodium sulphate appear to sustain this view.

The action of sodium sulphate, however, in this connection is probably not a chemical one, as has been conclusively proved by Tauber. The action must probably be due to the hindering of absorption and possibly also to purgation of the animal. For the same reasons magnesium sulphate could be used, but its use is to be discouraged on account of the possibly depressing effect of the magnesium ions, in case of their absorption.

On the Rôle of Alcohol in Phenol Poisoning.

The unfavorable action of alcohol in cases of carbolic-acid poisoning just noted seems to be contrary to the popular experience with this form of poisoning. Most of us have seen or heard of cases in which whiskey had apparently saved a man from death by carbolic acid. As an example, I will quote a news item, which I have very recently cut out of a paper, and which will serve as a good illustration of what I mean:

Robert C., 24 years old, because he could not find work, drank carbolic acid here last night. C. first drank whiskey to stupefy himself before taking the poison. The whiskey in a measure counteracted the effect of the deadly drug. He was found by his wife lying in bed writhing in agony. C. was quickly rushed to the hospital, where he is still suffering.

Such cases are not fakes. I have seen them myself. How can we reconcile them with our experimental data? To clear up the problem, the idea suggested itself to try the following experiments:

Exp. 47. July 21, 1914. Kitten A. Wt. 0.7 kg.
Introduced into stomach 1 cc. of 95 per cent alcohol diluted with 10 parts of water. 15 minutes later introduced 1 cc. more of 95 per cent alcohol diluted with 10 parts of water. 1 hour later, the animal was found to be thoroughly drunk. It could not stand on its feet, and was drowsy. The heart and respiration, however, were regular and good. 0.7 cc. of a 10 per cent solution of carbolic acid was then introduced into stomach.
Convulsions appeared in 5 minutes. The animal's stomach was then washed with 500 cc. of plain water. The pulse and respiration continued good and the animal made a rapid and perfect recovery. It was well and was used for another experiment the next day.

Exp. 48. July 21, 1914. Kitten B. Wt. 1.2 kgs.
Introduced 1.2 cc. of 10 per cent carbolic acid into the stomach. Clonic convulsions set in 2 minutes later. Washed immediately with 500 cc. of 15 per cent alcohol, followed immediately by plain water. Heart and respiration stop and animal succumbs in a few minutes.

Exp. 49. July 22, 1914. Kitten C. Wt. 0.8 kg. Washed the stomach with 500 cc. of 15 per cent alcohol, followed immediately by 500 cc. of plain water.
No convulsions noted. Animal goes to sleep; wakes up 2 hours later and is perfectly normal.

On comparing these three experiments it will be seen that Kitten B, which received 0.1 cc. per kg. of liquid phenol, developed convulsions in 2 minutes, and succumbed after prompt lavage with alcohol, followed by water.

Kitten A, which was previously thoroughly intoxicated with alcohol and then received a similar dose of phenol, de-

veloped convulsions later, that is, 5 minutes after the introduction of the poison; but its heart and respirations continued good, and it recovered after lavage with plain water.

That washing with alcohol alone will not kill an animal is shown by the control experiment on Kitten C.

An exactly parallel series of experiments with exactly similar results was made on dogs, as shown by the following protocols:

EXP. 43. July 27, 1914. Dog A. Wt. 11 kgs. In good condition.

10.00 a. m. Given 20 cc. of 95 per cent alcohol diluted with 5 parts of water.

2.00 p. m. Thoroughly drunk and drowsy; salivated.

2.20 p. m. Introduced 5.5 cc. pure carbolic acid in 10 times its volume of water.

2.25 p. m. Slight tremor and weak convulsions.

2.35 p. m. Washed stomach thoroughly with water until smell of phenol could not be detected. Pulse and respirations good.

Taken off the table unconscious and trembling, but in fair condition. Recovery next day.

EXP. 37. July 27, 1914. Dog B. Wt. 8 kgs. In good condition.

2.25 p. m. Introduced 4 cc. of pure carbolic acid in 10 times its volume of water.

2.28 p. m. Convulsions appear.

2.40 p. m. Washed stomach with 1 litre of 15 per cent alcohol, followed immediately by water.

Heart and respirations stop suddenly. Dog dies on table.

EXP. 44. July 27, 1914. Dog C. Wt. 7 kgs. In good condition.

Washed stomach with 1 litre of 20 per cent alcohol, followed immediately by 1 litre of water. Taken off table conscious and in good condition. Next day, normal.

The following protocol shows that in a previously alcoholized dog recovery is possible even after an enormous dose of carbolic acid:

EXP. 46. July, 1914. Dog. Wt. 5.4 kgs.

Given 10 cc. of 95 per cent alcohol in 10 parts of water. One hour later 10 cc. more of 95 per cent alcohol in 10 parts of water. When the dog was thoroughly narcotized, one hour later, 5.4 cc. of pure carbolic acid, *i. e.*, 1 cc. per kg., or twice the fatal dose, were introduced into the stomach, mixed with 5 parts of water.

Slight convulsions set in in 4 minutes. Lavage with plain water was then begun. The heart and respirations did not fail throughout the operation. The dog was taken off the table unconscious, and showed a tremor but no violent convulsions. One hour later the animal was seen walking around and in pretty good condition, no worse for his experience.

These experiments, as well as a sufficient number of others which I need not give here in detail, bring out the very interesting fact that there was a very great difference in animals which had previously received alcohol and subsequently phenol, and those in which the administration of alcohol was subsequent to or simultaneous with that of the phenol. Hence we may conclude that animals which have been previously poisoned with alcohol are able better to withstand the action of phenol. What the explanation of this curious phenomenon is is not quite clear, but the result is probably due to the greater affinity of the alcohol for the nerve cells, which prevents the phenol from getting hold of them. The effect of alcohol *after* the ingestion of phenol is simply to promote still further absorption of the acid as it acts as an excellent solvent for phenol. Dr. Turner, of the pharmacological laboratory, suggests that the difference of the effect in the two cases may further be explained on the theory of surface tension.

It was interesting to find that the same conditions hold good after the *subcutaneous* administration of alcohol and phenol.

For this purpose I utilized smaller animals, namely, white rats and kittens. The following protocols will illustrate the findings:

EXP. 57. Oct. 24, 1914. White rat. Wt. 90 gms.

2.00 p. m. Injected under skin 25 mgs. of phenol in 5 per cent solution.

2.04 p. m. Tremor noted.

2.06 p. m. Clonic convulsions begin.

2.25 p. m. Very rapid convulsions, too rapid to count.

2.30 p. m. Convulsions 168 per minute.

3.00 p. m. Same.

4.55 p. m. Death.

EXP. 58. Oct. 24, 1914. White rat. Wt. 65 gms.

2.02 p. m. Injected under skin 2 cc. of 10 per cent alcohol.

2.20 p. m. Animal distinctly drunk but conscious.

2.21 p. m. Injected 50 gms. of phenol in 5 per cent solution.

2.26 p. m. Convulsions begin but are not as rapid as in other animal.

2.30 p. m. Convulsions 140 per minute.

3.00 p. m. Convulsions slower.

6.00 p. m. Still alive.

Found dead next day.

EXP. 51. Oct. 20, 1914. Kitten. Wt. 0.8 kg.

1.25 p. m. Injected 2 cc. of 5 per cent carbolic acid.

1.26 p. m. Tremor noticeable.

1.27 p. m. Clonic convulsions.

1.38 p. m. Coma and rapid convulsions.

1.45 p. m. Same.

2.00 p. m. Same.

2.45 p. m. Same. Injected 2 cc. more of 5 per cent carbolic acid.

3.30 p. m. Very violent convulsions.

6.00 p. m. Exhausted.

9.00 p. m. Death.

EXP. 52. Oct. 20, 1914. Kitten. Wt. 0.7 kg.

12 m. Given 3 cc. of 95 per cent alcohol in water.

1.15 p. m. Animal distinctly drunk.

1.25 p. m. Injected 2 cc. of 5 per cent carbolic acid.

1.27 p. m. No convulsions.

1.38 p. m. Slight tremor but no convulsions.

1.45 p. m. Tremor but no convulsions.

2.00 p. m. Slight convulsions noted.

2.30 p. m. Same.

2.45 p. m. Injected 2 cc. more of 5 per cent carbolic acid.

3.30 p. m. Very little change.

6.00 p. m. Convulsions getting stronger.

10 p. m. Convulsions continued.

Found dead next day.

It can be pretty safely assumed that the above experiments furnish an explanation for the conflicting opinions in respect to the value of alcohol in carbolic-acid poisoning. A previously drunken person will probably withstand the ravages of phenol better, whereas one that takes carbolic acid mixed in alcohol, or victims of phenol poisoning washed or doused with alcohol for therapeutic purposes, are more liable to perish. Thus it is interesting to note that of ten cases (mentioned by Falck [21]) of carbolic-acid poisoning where the victims

drank carbolic acid in various alcoholic drinks, such as schnapps, brandy, rum, or beer, 9 of the 10 succumbed; whereas of 17 persons who drank carbolic acid simply by mistake, only 13 died.

The practical importance of this fact cannot be overestimated, for on the one hand we frequently read news items, such as the one quoted above, and on the other we still find standard works on toxicology which advise the administration of alcohol in carbolic-acid poisoning. Thus one of the most popular American text-books on Legal Medicine and Toxicology says:[23] "Alcohol is the best antidote. When the poison has been swallowed whiskey may be taken with advantage." And in one of the standard American reference works on toxicology we read the following:[23] "It seems very probable that the best method of treating a case of carbolic-acid poisoning would be to administer alcohol, provided the stomach be washed out immediately afterward." It was therefore with great pleasure that I read in another recent text-book by Holland[24] the statement based on purely chemical grounds: "Dependence should not be placed on alcohol as an antidote."

Summary.

1. The efficiency of lavage in phenol poisoning depends on the quantity of poison taken, on the time after poisoning that the lavage is begun, and on the solution used for washing the stomach.

2. A strong solution of sodium sulphate appears to be the most useful for the purpose; next in efficiency comes plain water.

3. The influence of alcohol in phenol poisoning depends on the time of its administration. An animal that is previously intoxicated with alcohol can withstand better the effects of phenol taken afterwards. On the other hand, alcohol administered to an animal after poisoning with phenol will aggravate the symptoms and hasten death.

4. The use of alcohol in carbolic-acid poisoning should therefore be strongly discouraged.

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THE BEGINNINGS OF MEDICINE IN THE MIDDLE WEST.*

By Otto Juettner, M. D., Ph. D., Cincinnati, O.

The story of the birth and development of medical thought and practice in the interior valley of North America is closely interwoven with the inception and growth of Western education and culture. The men who were the pioneers of medical art and science in the Western country were, almost without exception, men of affairs who stood in the foreground of public life and crystallized the genius and the ideals of their time and their country in a characteristic manner. They were not only the makers of medicine in the West, but contributed in no inconsiderable degree to the social and educational history of our republic. Whatever there is of great and momentous power in American history, is in many instances closely affiliated with the names of illustrious physicians who were the standard-bearers of civilization in those early days, and not only helped to mould the character of our profession, but were the leaders in the eternal struggle for the altruistic ideals of humanity.

* Read before The Johns Hopkins Hospital Historical Club, November 9, 1914.

The early beginnnings of medicine in the Middle West were coincident with the dawn of the nineteenth century. The century was only nine years old when an event of the greatest historic moment established Western Medicine as a distinct chapter in the annals of medicine generally. In 1809 Ephraim McDowell made his memorable contribution to the possibilities of operative surgery. It was an event of far more than ordinary importance and, considering all the circumstances, may be accepted as a distinctly Western achievement. McDowell came to the pioneer settlement of Danville, Ky., when he was 13 years of age. He developed into a Western doctor of the early times—shrewd, resourceful, dignified, truthful, and replete with the academic flavor which his training under John Bell, of Edinboro, had given him. McDowell's ovariotomy in 1809 undoubtedly meant a great display of courage as well as of anatomic and pathologic knowledge. Some say it was one of the greatest feats in the history of surgical art. Inasmuch as it paved the way for the entire subject of abdominal surgery in the treatment of diseases of women,

McDowell's operation is not likely to lose much of its glamour by historic or any other kind of analysis. But this is not the point that is of consequence to us on this particular occasion. I want to emphasize to you the fact that Ephraim McDowell was a Western doctor and that his historic operation in 1809 was the first awakening of scientific medical thought on the other side of the Alleghany Mountains. The name of McDowell has such a familiar ring and the history of his great work has been told so well and so often that I can assume familiarity with it here, where the work, begun by that great pioneer-surgeon, has been evolved and developed as much as, if not more than, anywhere on this continent. I could not add any new immortality to the name of the father of ovariotomy by again telling the story of his work.

What preceded him and his work in the newly colonized West, say after 1785, was of no characteristic import. The pioneer-settlers were the carriers of civilization and many doctors, mostly from the East and perhaps officially attached to some of the military posts in the West, practiced medicine among the settlers. Most of them were not graduate physicians. There were no schools of medicine in the new territory and only one in the East. A good type of the itinerant Western doctor of early times was Peter Smith, originally a New Jersey man, who went to Virginia with a B. A. from Princeton, and began to preach the gospel to the new colonists. He lingered for a time in Virginia, then in the Carolinas and finally settled in Georgia as an old-fashioned Baptist minister. Being a strong anti-slavery man, even in those early days, he found himself in continuous trouble with his neighbors, who were all slave-holders. He decided to leave and began to meander through the country with his family. His wife sat on a big horse; the two smallest children slept in baskets hung to the horns of the saddle, the other children, thirteen in all, walking along on either side of the horse. Smith traversed Georgia, Tennessee and Kentucky in this fashion. He was disgusted with the slavery he found everywhere and decided to leave the South and its scorpions, head-ticks, bad whiskey and slaves, as he expressed himself. He came to Cincinnati about 1794 and preached in the old Baptist church on Duck creek, near Cincinnati. After some years he moved to Donnell's Creek, Ohio, and became a farmer. He died here in 1816.

Smith was the son of a physician and in traveling from place to place, picked up bits of medical knowledge. He was particularly interested in the medical notions of the Indians, and eventually expanded his work by becoming a healer of the body in addition to being a minister of the soul. In 1812, while engaged in missionary work in Cincinnati, he published a book on his methods of practice under the title of "The Indian Doctor's Dispensatory." This book, written by this picturesque itinerant doctor, is the first book on medicine published in the West. It is a curious publication, containing crude and strange medical superstitions and vagaries, and, with it all, much knowledge of the pathology of diseases and the physiological action of remedies. Smith is a strong advocate of sunlight, fresh air and water and a great believer in the curative properties of the herbs used by the Indians. It is interesting to know that Rafinesque, who wrote on American plants many years later, quotes Smith very liberally and attaches much importance to his views. There are not more than three copies of Peter Smith's book still in existence. The Lloyd Library, of Cincinnati, has recently published it for the benefit of the many who are interested in the medical history of the West. Smith's Dispensatory was published in 1812. There was at that time very little of American medical literature to be found anywhere. When Smith's book appeared in Cincinnati not more than a dozen books on medicine had been written by Americans. Dorsey's Surgery and Wistar's Anatomy, at one time the most popular American books on their respective subjects, had not yet made their appearance. Peter Smith must have been a man of close observation and great originality, judging by the character of his work, no less than by the mere fact of publishing a book on medicine at a time when he could not help being original. Thus, he is a noteworthy character in American medicine and is entitled to a more respectable position in our history than has thus far been accorded to him. As I have stated, he was an herb-doctor or botanical practitioner. Men of this type, as you know, made a good deal of noise one hundred years ago. Peter Smith undoubtedly was one of the most original and interesting characters among these exotic products of the early times. I regret that I cannot show you a likeness of Peter Smith, the Indian doctor. There is no picture of him extant. The burial-place of this quaint and original pioneer is in a pitiful state of neglect. I have recently tried to interest the profession of Ohio in the memory of Peter Smith. We hope to soon be able to place a suitable memorial tablet on his grave to remind the present generation of the first medical author in the history of the West.

The events of the formative period of medicine in the West can be conveniently grouped around the gigantic figures of three men who loomed up approximately at the same time and influenced the development of medicine in a very direct and characteristic manner. One of them I have already mentioned. He was Ephraim McDowell, of Danville, Ky., whose ovariotomy in 1809 opened a new chapter in surgery and incidentally inaugurated the history of medicine in the West. McDowell did a great deal of creditable work and, while he was not connected with any of the early Western schools of medicine, trained and educated a number of young men who became great medical teachers and leaders of the profession in different parts of the country. One of his assistants, Alban Goldsmith, was one of the pioneers of genito-urinary surgery in this country and is remembered as professor of surgery at the New York College of Physicians and Surgeons. He was born and bred in Louisville, and owed his New York appointment to his great surgical ability. He witnessed McDowell's first operation and repeated the operation successfully on a number of occasions. McDowell died in 1830. His operation fell into disrepute after his death and the fruits of his labors would have been lost if it had not been for the work done by Alexander Dunlap, of Springfield, Ohio, who,

twelve years after the master's death, performed the classical ovariotomy of McDowell and precipitated an unparalleled avalanche of condemnation among the profession. Dunlap stuck to his post and convinced the profession by hundreds of good results that McDowell had really been a pathfinder in the interests of the human race. That McDowell's name and work were saved, we owe to the heroism and matchless professional ability of Dunlap and of his distinguished Eastern collaborator, Washington Atlee, of Philadelphia, whose name is likewise linked to that of the great Danville surgeon for all time to come.

I stated that the early medical history of the West was grouped around the heroic figures of three great men. McDowell, being the center of his own special activity, naturally remains in a class by himself. The other two men worked in the interests of medical education and became leaders of the profession along different lines. These two men, whose gigantic figures loom up in silent and solemn grandeur at the very inception of the story of Western civilization, seem larger and more imposing after the elapse of nearly a century and have long become landmarks, not only in the West, but in the United States, being among the most distinguished characters in the annals of medicine in America. One of them is Benjamin Winslow Dudley, the founder of the medical department of Transylvania University in Lexington, Ky.; the other is Daniel Drake, that wonderfully versatile and brilliant man who established the Medical College of Ohio in Cincinnati in 1819. The life work of these two eminent medical educators, more especially that of Drake, forms one of the brightest pages in in the history of American medicine and was of incalculable service to the cause of civilization in that unexplored territory which, a century ago, was one vast empire of barbarism.

Benjamin Winslow Dudley, the father of the medical school in Lexington, Ky., was born in Virginia in 1785, but came to the pioneer town of Lexington when he was only one year old. Here he remained, lived, worked and died at the ripe old age of 85 years. He studied medicine at the medical department of the University of Pennsylvania. Young Dudley was an impressionable and ambitious student who drew no end of inspiration from the teaching of the famous men who composed the Philadelphia faculty. He graduated in 1806 and hastened back to Lexington to offer his friends and neighbors his stock of newly acquired knowledge. His ambition was to be a surgeon, but he waited in vain for patients who were willing to let him try his surgical skill on them. Dudley was poor and found himself compelled to adopt some method of keeping the wolf from the door. He purchased a flatboat, loaded it with produce, headed it for New Orleans, and floated down the Kentucky, the Ohio and Mississippi rivers to the desired port. He invested the proceeds of his cargo in flour. This he billed to Gibraltar, which he reached some time in 1810; there and at Lisbon he disposed of it with large profits. The liberal supply of filthy lucre in his pocket reawakened his medical ambition. He went to Paris and London and sat at the feet of the great masters of surgery. With new hopes and greater ambition than ever he returned to Lexington, where a disastrous epidemic of malignant typhus was raging. His European prestige proved to be quite a drawing card. Everybody wanted to be treated by the man who had studied in Paris and London. Thus Dudley in a few years became a famous physician and surgeon. In 1817 the trustees of Transylvania University in Lexington conceived the idea of adding a medical department to their institution and drew Dudley into their confidence. The word "Transylvania," as you may remember, was the original name of the colony which eventually developed into the state of Kentucky. When, in 1770, the charter for a seminary in Lexington "for the teaching of the higher branches of learning" was granted, it was decided to perpetuate the historic name by calling the new school "Transylvania Seminary," and afterwards "Transylvania University." Dr. Dudley was made the head of the medical department and at once proceeded to organize a faculty. The rise of this school, the first medical school in the West, was most auspicious. Lexington was noted for its culture and urbanity. It had 8,000 inhabitants, among them some wealthy people who, in addition to their shekels, had plenty of local patriotism to help the town along. Lexington was generally called the "Athens of the West," and nobody questioned its ultimate supremacy as the leading city in the Ohio Valley. Cincinnati at that time had 10,000 inhabitants, mostly workingmen, who had collected from all parts of this country and Europe and, of course, could not cope with their neighbors in Lexington, either in wealth or education. Compared to Cincinnati, a typical Western pioneer town, Lexington, with its wealth and fine colonial mansions, appeared like a metropolis. Yet, Cincinnati began to be well known in many places. A little pamphlet had appeared in 1810 which gave much information about the town and proved to be a mighty effective advertisement, especially in the East, where the pamphlet was eagerly read by people who intended to try their fortunes in the West. In 1815 a pretentious little volume appeared which gave still more definite information about Cincinnati, its topography, climate and municipal and civic possibilities. This book, called "Picture of Cincinnati", found its way to Europe, where parts of it were translated and published for the benefit of prospective emigrants. The author of the aforesaid pamphlet, as well as of the "Picture of Cincinnati," was a young physician whose name I have already mentioned. He was destined to become one of the greatest figures in American medicine and cannot inappropriately be called the Father of Western Medicine, namely, Daniel Drake. When Dudley was casting about for material to organize the Transylvania medical faculty he thought of Drake and offered him a professorship in his school. To be a professor in a medical school in the West was such a novel distinction that Drake did not hesitate for a moment to accept the offer. Before saying anything more about Dudley and his new school at Lexington, it seems proper to pause for a few moments and think of Drake, who, aside from his medical achievements, is the one really great character whose name is associated with the advance of civilization in the Ohio Valley and in the upbuilding of the entire West.

Drake and Dudley were born in the same year, 1785. Drake

was born in New Jersey and was about two years old when his father came West to locate near Maysville, Ky. Here young Drake was reared amid scarcity of money, but wealth of virtue, until he was 15 years of age, when his father arranged to send him to Cincinnati to study medicine under a typical doctor of colonial times, Dr. William Goforth. In 1805 Dr. Goforth made Drake a full-fledged doctor of medicine by granting him a diploma, the first diploma received by a medical student in the West. Later on Drake took a course in the medical department of the University of Pennsylvania and received the degree of doctor of medicine. In 1817 Drake left Cincinnati and went to Lexington as a member of the medical faculty of Transylvania University. Incidentally let me call attention to that splendid historical book, "Pioneer Life in Kentucky," in which Drake described his early childhood in the Blue Grass State. It is a book which everyone who is interested in the history of the West should read.

In connection with the early history of Cincinnati it is of interest to know that the two names of the town, namely, Losantiville and Cincinnati, were suggested by two men who were closely related to the medical profession. John Filson, who invented the first name of the town, namely, Losantiville, was a medical student and intended to locate as a physician in Lexington, Ky. "L" is the first letter of the word "Licking," the name of a Kentucky river, "anti" means opposite, "os" mouth and "ville" town. Thus Losantiville means "the town opposite the mouth of the Licking." Unfortunately Filson's career came to an untimely end before he had a chance to carry out his plans. The name of "Cincinnati" was the suggestion of General Arthur St. Clair. He wanted to thus honor the patriotic order of the "Cincinnati," of which he was a zealous member. Before the fortunes of war tempted him to become a soldier, he had studied medicine for one year in London under John Hunter.

The story of the medical department of the Transylvania University, especially the first decade of the school, presents a composite product of every phase of human emotion from the heroically sublime to the grotesquely ridiculous. It reads like an epic poem when the achievements of the really great men are referred to, who composed the faculty, beginning in 1817. Dudley was a tremendously able man, but he was intensely human. This fact injects much pathos and still more humor into the narrative. Thundering Jove was not a greater autocrat in the affairs of Olympus than Dudley was in the management of the Transylvania school. He was a giant in stature, had an awful temper, and when aroused, used language in the faculty room that laid no claim to elegance, while its force could not possibly be questioned. He was fond of emphasizing his remarks with his fist, which he would use with telling effect on the faculty table. Some of the professors were Kentuckians who did not take kindly to this mode of argumentation. The result not infrequently would be a fisticuff engagement in which Dudley usually held his own. He used surgical instruments with consummate skill, but in true Kentucky style he was also very handy with a gun. One of the distinguished professors associated with Dudley was Wm. H. Richardson, a typical Kentuckian, who came from an excellent family and was a very scholarly man. During one of the faculty meetings Richardson criticized some suggestion which Dudley had made. Dudley told him that if he did not keep his mouth shut he would shoot his ——— head off. Richardson told him he would meet him at any time and accordingly a duel was arranged. The two gentlemen shot at the same moment. Richardson's bullet went astray, while Dudley's bullet struck Richardson in the leg, severing the femoral artery. Richardson would have bled to death if Dudley had not come to the rescue by ligating the artery. After the operation the two antagonists shook hands and were good friends ever after. In spite of this and similar occurrences, the medical school of Transylvania flourished and was for fully three decades one of the great American colleges of medicine. In 1826 the class numbered 235 students. Among the professors were some of the most distinguished medical men of their time. Dudley was a tower of strength. In spite of his erratic manner, he enjoyed the respect of his colleagues on account of his great ability as a surgeon. He performed more than 600 lithotomies with a mortality of only 4 per cent; and all this before the days of anesthesia and surgical cleanliness. This record alone stamps him as one of the immortals in the history of surgery. Another strong man of the faculty was Charles Caldwell, who was a wonderfully productive writer and was thought to be one of the (if not the) most learned American physicians of his time. His clever speculations on phrenology won him many admirers at that time and make good reading even to-day. Then there was Charles Wilkins Short, who had a national reputation as a botanist, and who is still remembered because some American plants bear his name. There were many other distinguished medical teachers connected with Transylvania. In 1839 the city of Lexington erected a special building for the medical school. About 1860 the medical department of Transylvania was abandoned. During its brilliant career more than 2000 American physicians had received their degree at the old school. The grim old warrior who had founded it, outlived it by ten years. He died in 1870.

During the thirties some of the medical professors of Transylvania seceded and joined the Louisville Medical Institute, which, after 1840, rose to great prominence. Daniel Drake taught at this school from 1840 to 1850. Samuel D. Gross, who afterwards rose to one of the most exalted stations in American medicine as professor of surgery in Jefferson Medical College of Philadelphia, was also connected with the school for a number of years. Lunsford P. Yandell, the professor of chemistry, had a great reputation in his day. This school was the prolific mother of a number of small medical colleges in Louisville that came, saw, and were finally absorbed into the medical department of the University of Louisville.

I mentioned the fact that Daniel Drake was one of the early professors in the Transylvania school. He remained just one year. One season with Dudley was all he could stand. Drake returned to Cincinnati in 1848 and at once got busy planning a medical college in Cincinnati. The result of his

activity was the Medical College of Ohio, which began a most tempestuous career in 1819. Within two years after the college had sprung into existence, Drake was expelled by his own faculty. The faculty consisted of Drake, Jesse Smith, professor of surgery, and Elijah Slack, the president of the old Cincinnati College, who taught chemistry. These three men were their own trustees and when trouble arose about some minor matters, Smith and Slack decided to expel Drake, which was accordingly done. Drake described this serio-comic episode in a pamphlet entitled "The Rise and Fall of the Medical College of Ohio." The pamphlet is a classic of its kind and shows the versatile Drake in a new rôle, that of a delightfully keen humorist. No physician who is interested in the medical history of the West should forego the pleasure of reading this unique document. I would not be doing my subject justice if I did not by way of a short quotation give you an idea of Drake's delicious humor. Drake tells the story of his expulsion in the following manner:

> At 8 o'clock we met according to a previous agreement, and transacted some financial business. A profound silence ensued, our dim taper shed a blue light over the lurid faces of the plotters, and everything seemed ominous of an approaching revolution. On trying occasions Doctor Smith is said to be subject to a disease not unlike St. Vitus' dance, and on this occasion he did not wholly escape. Wan and trembling, he raised himself (with the exception of his eyes) and in lugubrious accents said, "Mr. President, in the resolution I am about to offer, I am influenced by no private feelings, but solely by a reference to the public good." He then read as follows: "Voted that Daniel Drake, M. D., be dismissed from the Medical College of Ohio." The portentous stillness recurred, and was not interrupted till I reminded the gentlemen of their designs. Mr. Slack, who is blessed with stronger nerves than his master, then rose, and adjusting himself to a firmer balance, put on a proper sanctimony and bewailingly ejaculated: "I second the motion." The crisis had now manifestly come; and, learing by inquiry that the gentlemen were ready to meet it, I put the question, which carried, in the classical language of Doctor Smith, "*nemo contradicente*." I could not do more than tender them a vote of thanks, nor less than withdraw, and, performing both, the doctor politely lit me downstairs."

After his expulsion Drake spent most of his time getting even. In 1831 the trustees of Miami University, of Oxford, Ohio, arranged with Drake to open a medical department in Cincinnati. Drake brought some excellent talent to Cincinnati, mainly from the East. The most distinguished medical teacher who was given a chair in the prospective medical department of Miami University was John Eberle, who came from Hagerstown, Md., and was lecturing at Jefferson Medical College when Drake asked him to come West. A very promising young man was Jas. Staughton of Washington, D. C., who was a graduate of the University of Pennsylvania and had spent two years in Europe studying under famous English and French surgeons. Upon his return he taught surgery at the Medical Department of Columbian College, of Washington, D. C., and attracted a great deal of attention as an eloquent and resourceful teacher. When Drake invited him to come to Cincinnati, he at once acceded and became the professor of surgery in the Medical College of Ohio. He died of cholera in 1833. He wrote two monographs possessing great merit, one on "The Life and Services of Ambroise Paré," the other on "The History of Lithotomy."

Of the Eastern men who in the early days had come West to share in the work of establishing the science and profession of medicine, no one occupied a more honorable position East or West than John D. Godman, who was a native of Annapolis, Md., and was a graduate of the University of Maryland. He became the leading American anatomist of his time. Like Bichat of France, he died young, but his name will live as long as the cause to which he gave his efforts is not forgotten. Godman remained in Cincinnati but one year. He was a lover of peace and not a well man. He was, therefore, hardly prepared to prosper amid the stress and strife of the early existence of the Medical College of Ohio. While in Cincinnati he published the "Western Quarterly Reporter of Medical, Surgical and Natural Science," the first medical journal in the West. Godman, as you know, became professor of anatomy in Rutger's Medical College after he left Cincinnati. He died at the age of 36, young in years but old and mature in scholarship and intrinsic value and quality of creative activity. Another man who was a teacher in the Medical College of Ohio in the early days was Benjamin S. Bohrer, who came from Washington, D. C., and after a turbulent experience in Cincinnati, returned to his native town, where he rose to great distinction as a learned and cultured member of the profession. A noteworthy figure among the early professors was Jedediah Cobb, a New Englander, who was a great anatomist as well as an artist of ability. He was the first man in this country who gave a systematic course in plastic anatomy.

The plan conceived by the Miami University trustees miscarried most disastrously. To meet the dangers of the unexpected competition, a reorganization of the Medical College of Ohio was effected by the trustees of the latter and, in some manner or other, the newly imported professors of the Miami University Medical School were induced to join the Ohio College. When he saw that the scheme had failed, Drake meekly joined the procession and again became a teacher in the school which he had founded in 1819. At the end of the session he resigned and decided to try another plan to set himself right with the world. The old Cincinnati College listened to Drake's eloquent pleading and opened a medical department in 1835. This school was the climax of Drake's career as a builder of institutions of medical learning. It has been said that this school, which was abandoned in 1839, marked the highest point reached by medical education in the West. The men whom Drake assembled in this great school, were all national celebrities and stars of the first magnitude in their respective lines of work. They were such men as Samuel D. Gross, who in after life as professor of surgery at Jefferson became one of the great surgeons and authors of his time; Willard Parker, who, later on in New York, became a distinguished surgeon: Horatio G. Jameson, one of the founders of Washington Medical College, of Baltimore, Md., one of the most eminent surgeons of his time who will always be remembered as the man who introduced animal ligatures into surgical practice; Joseph Nashe McDowell, Ephraim

McDowell's nephew, founder of the first medical college in St. Louis, matchless orator, brilliant anatomist, famous surgeon of whom Henry Clay once said that he had more brains and less common sense than any doctor in America; and James B. Rogers, afterwards professor of chemistry in the University of Pennsylvania. Men of this caliber were Drake's associates in the Cincinnati College. The school collapsed after four years of glorious existence because it had no facilities for giving bedside instruction. It was barred from the old Commercial Hospital because only the professors of the Medical College of Ohio, which was a state institution, had access to the hospital. The humor of this situation becomes apparent when it is remembered that Drake founded this hospital in 1820.

In spite of difficulties and hardships without end the Medical College of Ohio soon became a formidable rival of the Transylvania school. One of the first graduates of the Ohio College was John L. Richmond, who originally came from New York, but drifted to Cincinnati and became the janitor of the Medical College of Ohio. He worked day and night and finally succeeded in obtaining the degree in medicine. He located in Newtown, Ohio, about ten miles from Cincinnati, and, being a Baptist minister, looked after the physical as well as the religious welfare of the people of Newtown. In 1827 he performed a Caesarean section under the most trying circumstances, saving the life of the mother. *This case is the first authenticated case of its kind in this country.* I had the good fortune of presenting the life and services of Dr. Richmond to the medical profession of Cincinnati, and succeeded in arousing considerable interest. The result was the erection of a monument commemorating Dr. Richmond's famous Caesarean section, in Newtown, O.

In 1827 the first building in the West devoted to medical teaching arose on Sixth street, near Vine, and was the home of the Medical College until 1852, when a larger building took its place. Among the teachers of the Ohio College, even before 1840, were some very eminent men, notably Reuben D. Mussey, the great surgeon; Jared Potter Kirtland, who afterwards went to Cleveland and became one of the great naturalists in the West; and John Locke, the inventor of the electric clock, whose name is known to every American student of the natural sciences; Marmaduke B. Wright, the originator of bi-manual version; Henry Willis Baxley, the founder of the Baltimore College of Dental Surgery, the first dental school in the world, and, last but by no means least, Roberts Bartholow, who saw the light of day in Maryland, became a great medical figure in Ohio and was given back to the East when he had become the leading American therapeutist of his time.

The history of medical schools in the Ohio Valley is not without its humorous features. The short-lived career of the Evansville, Ind., Medical College (chartered in 1846) was a product of the religious fervor and temperance agitation in those days. Classes were opened with prayer and lessons in anatomy made more interesting by the interjection of an occasional Bible-reading. Students who promised not to use liquor, tobacco and profane language were admitted without having to pay any tuition. The average medical student found these requirements too exacting. Thus, the school soon closed its doors. After 1823 medical colleges began to multiply in all parts of the country. Joseph Nashe McDowell, brother-in-law of Daniel Drake and nephew of the great ovariotomist, Ephraim McDowell, started the Missouri Medical College in St. Louis in 1840. In 1841 Charles Pope, a Cincinnati graduate, organized the St. Louis Medical College, which enjoyed a long and prosperous career, and in 1891 became the medical department of Washington University. In 1843 Rush Medical College in Chicago started on its honorable career. In the same year (1843) the Cleveland Medical College, the forerunner of the medical department of the Western Reserve University, was founded. Starling Medical College, Columbus, Ohio, followed four years later. In 1849 the medical department of the University of Michigan, at Ann Arbor, was organized. The Cincinnati College of Medicine and Surgery and the Miami Medical College, both of Cincinnati, were founded in 1851 and 1852, respectively. They have both passed out of existence. The cause of death in the former was marasmus, brought on by medical legislation, which raised the educational requirements for medical students and thus reduced the patronage of medical schools. In the case of the Miami College the final dissolution, euphemistically speaking, was accomplished by a more or less amicable absorption into the University of Cincinnati. It was the humane ending of a long and honorable career.

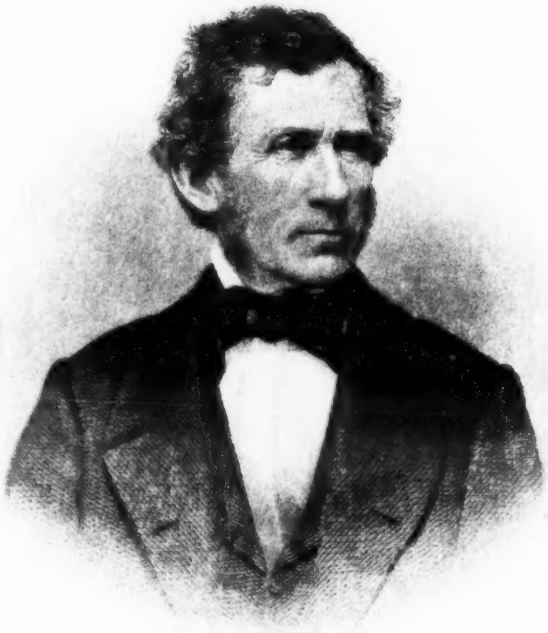
The question of the share which the West can rightfully claim in the sum total of achievement represented by American medicine cannot easily be answered. The medical West naturally is a derivative of what preceded it. The roots of our accomplishments were in the East. Most of our great physicians and teachers, like Daniel Drake, had the seal of approval set upon them by that undisputed alma mater of American medicine, the University of Pennsylvania. In following the development of medical education on American soil we cannot help but appreciate the tremendously vital part played by Philadelphia in furnishing material, inspiration and life itself to the cause from the earliest times. And in all this wonderful activity of mind and heart there appears the personality of Benjamin Rush, the artist whose beck and call and fine appreciative touch gave life to the picture that was created in those heroic days. As we peer down through the aisles of time, he seems so much greater and more imposing to us than he did to the men of his own time or to those immediately following him. To us he looks every inch a heroic figure of tremendous proportions with a classic, a Hippocratic perfection to every move, to every pose. Even his defects and mistakes appear impressibly sublime. That the work of such a man should have placed the impress of genius on the achievements of a whole century seems but a natural course of development. But what has this to do with the evolution of medicine in the West? Give your thoughtful attention to Philadelphia, to Benjamin Rush and to American medicine and see how complete and mutually supplemental this historical drama becomes, each part generating, containing and perfect-

ing the logic of the other two. History recognizes the towering greatness of Rush and places him at the side of probably a dozen other men who were, like Rush, originators of great movements in medicine. Having gazed upon the earliest events that accompanied the birth and heroic youth of American medicine, turn your eyes to the West and think of Cincinnati, of Daniel Drake, of Western medicine. The stage was larger, the appurtenances fewer and more crude, but what has the ultimate harvest been? In looking back over the early times of Western medicine, the one really great and tremendously persuasive factor is the figure of Daniel Drake. *He* is the subject that makes the whole chapter worth while. From whatever side you see him, in whatever manner you analyze him, as a man, as a teacher, as a writer, as a public character, he is a tremendously impressive and heroic figure. He would have made the same deep impression on a more elaborate stage with a more pretentious environment. He loved the West; he revered the stage-setting of his early childhood; he felt deeply for the people of the West, their ideals of life and patriotism; he was distinctly and characteristically a Western man. But everything he thought, said and did was great and powerful, never imperfect or provincial. As a man he impresses us with the childlike simplicity and sweet accordance of his character. As a medical teacher he stood before the students and doctors of medicine like a Daniel Webster, superlatively convincing in his logic and tremendously constructive even in his denunciations. As a public character he ranks with Henry Clay and will never be forgotten for the part he played in preparing public sentiment for the issue that found its final bloody settlement in the Civil War. As a medical writer he gave us the two-volume treatise on the "Diseases of the Interior Valley of North America." This work still occupies the rank which was accorded to it when it appeared, as being one of the few really original medical books written by Americans. If I were to attempt to tell you how this great work was prepared, my story would be an epic and Daniel Drake would be the hero. Like "Faust," which was the inspiration of Goethe's youth, the ever-present thought of his maturer years and the finished product of his ripe old age, Drake's great work was the realization of a dream which pursued its author throughout his whole professional life. The seed from which it sprang was the little book about Cincinnati which Drake published in 1810. Twelve years later he announced his intention to write his great work and asked the profession of the West to aid him in the gathering of material. Shortly after, he undertook the first of his extensive trips of observation, whih he continued year after year for almost a quarter of a century. He covered the whole Western country in these trips, studying the earth, the rivers, the plants, the animals, the air, the sky, the people. There were no authorities to quote from; no reference books to consult. He traversed the land in every direction on horseback, on foot, by boat or railway. He endured hardships and spent time, labor and money in the preparation and accomplishment of his great work. Appreciation is the life-food of genius. Daniel Drake lived long enough to receive it, because the reception of the work by the profession was certainly worthy of the effort and of the author. In 1850 the American Medical Association met in Cincinnati. Dr. Alfred Stillé, of Philadelphia, chairman of the Committee on Medical Literature, reported on the latest medical publications, and devoted the greatest part of his report to an analysis of Drake's work, referring to it as "an achievement of which every doctor in America should be proud." Drake was present and, upon arising, was greeted with a demonstration such as had never been accorded to any one on a similar occasion. The cheers and the clapping of hands were deafening and lasted for several minutes. Again and again the demonstrations started anew. Finally, when the noise had subsided, Drake wanted to thank his colleagues, but his voice failed him. He seemed to be growing faint and was helped to a chair. He covered his face with his hands and wept like a child. His friends crowded around him. To Dr. Stillé, who wanted to comfort him, he said, when he had gained his self-possession: "I have not lived in vain, but I wish father, mother and Harriet were here." In the hour of his greatest triumph, his mind reverted to his father, his mother and to the wife of his youth, all of whom had died many years before. It was Drake's unconscious apotheosis of himself.

Samuel D. Gross, who knew Drake intimately and has given us a very readable sketch of him, places Drake among the greatest men whom our profession in this country has produced. Gross pens a delightful word-picture of Drake's appearance about the time when he was lecturing at the Medical Department of the Cincinnati College. He was at that time 52 years of age and in full possession of his magnificent physical and mental powers. Gross tells us that Drake was a handsome man, with fine blue eyes and manly features. He had a commanding presence, being nearly six feet tall, having a fine intellectual forehead. His step was light and elastic; his manner was simple and dignified. He was always well-dressed, and around his neck he had a long gold watch chain, which rested loosely upon his vest. He was a great lecturer. His voice was clear and strong, and he had the power of expression which amounted to genuine eloquence. When under full sway, his whole soul would seem to be on fire. He would froth at the mouth, swing to and fro like a tree in a storm, and raise his voice to the highest pitch. With first-course students he was never popular, not because there was anything disagreeable in his manner, but because few of them had been sufficiently educated to seize the import of his utterances.

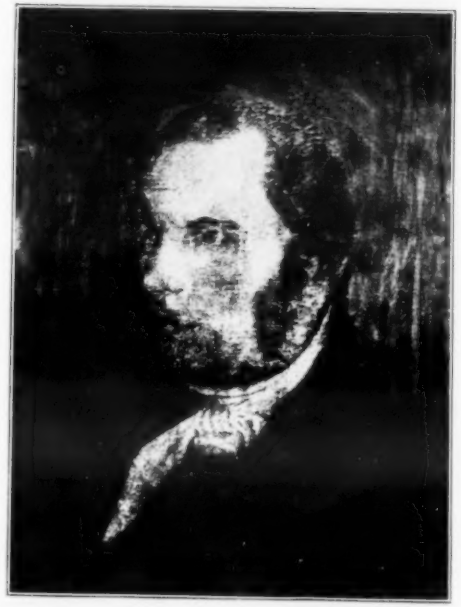
Gross characterizes Drake by saying he was easy of access, kind and genial, a hater of vulgarity and immorality, a lover of children and of innocent fun, a thoroughly noble Christian gentleman. His modesty bordered on affectation. In 1850 he refused the presidency of the American Medical Association because he did not think that he was worthy of such honor. He did not want to go to Europe because he was afraid of meeting great physicians, men of university education, who had had greater advantages than himself. "I think too much of my country to place myself in so awkward a position." Drake said this at a time when his name was spoken with respect everywhere in England and on the Continent.

Drake was himself in all things. When I say this about him,



DANIEL DRAKE

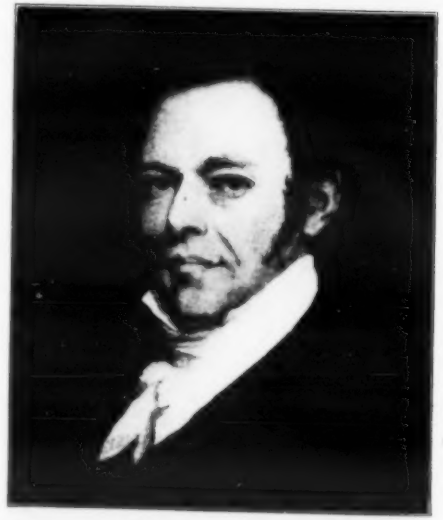
HARRIET SISSON DRAKE
(The wife of Daniel Drake)



JOHN L. RICHMOND
(The only picture extant. Reproduced from an old oil-painting)

ALEXANDER DUNLAP

THE RICHMOND MONUMENT AT NEWTOWN, O.



BENJAMIN WINSLOW DUDLEY

I must add that the love of Western people and Western ideals was a part of himself. When I have added this, I have given you a complete perspective of the man. When he went to Philadelphia in 1830, to lecture at the University of Pennsylvania, he was not too busy to look for and see things that might be of interest to his beloved Cincinnati. He found John Eberle and brought him, but long before this he had secured a soda-fountain which he brought to Cincinnati as a public attraction and to counteract the inroads of intemperance among the people. He loved Cincinnati and saw in her one of the great cities of the future. He loved her people because they were *her* people. He lived and loved in Cincinnati and the object of his life and his love was Cincinnati. The greatest acknowledgment of Drake's genius, however, should come from the members of his profession. Drake, above all things, was an American physician who spent his professional life in helping to develop all that is true and worth while in American Medicine. No physician from the West had as many friends and admirers in the East as he. Even in Europe his work as a naturalist was widely known and thoroughly appreciated. Towards the end of his life honors and distinctions were literally showered upon him, by the West as well as the East. Drake's labors were ended in the year 1852. In beautiful Spring Grove, Cincinnati's silent city of the dead, he rests beside his own beloved Harriet, beneath a modest shaft of sandstone which to-day is crumbling. Others, whose lives were of no import, have monuments of royal splendor.

And what has been the fruit of Drake's life and labor? The medicine of the West needs no apology. It has added much to our knowledge of practical resources in the treatment of disease. We can boast of a glittering array of Drake's followers who have continued the work of the master and have left footprints in the sands of time. The father of cholecystotomy, J. S. Bobbs, of Indiana, is one of the many distinguished examples of the medical genius of the West. Nathan Davis, of Chicago, gave us the American Medical Association which has united the disciples of Rush and Drake in the cultivation of the professional, scientific and patriotic ideals of our American profession. Let us not forget Wm. Beaumont, of St. Louis, the father of American physiology. The man who sat at the feet of Albrecht v. Graefe and carried the first ophthalmoscope to London and Paris, afterwards bringing it to this country, thus establishing modern ophthalmology as a distinct specialty, was Elkanah Williams of Cincinnati. Rush and Drake, and with them all the great leaders in American medicine who founded our medical schools East and West; men like Wm. Shippen, John Morgan, Philipp Physick, John Warren, Nathan Smith and John B. Davidge, radiate a specifically American form of public spirit and patriotism that has been of incalculable service, not only to the cause of medicine, but to the welfare of our country. In stepping before you and bringing you the greetings of the West I have tried to let *him* be my spokesman than whom no one understood the West better or loved his native land and all mankind more ardently.

To have been permitted to speak to you about the West and its professional childhood days, is indeed a priceless pleasure. To have had an opportunity of appearing before a distinguished audience of Eastern physicians and of paying homage to our Drake, whose superlative leadership has long been an inspiration to men like Samuel D. Gross, William Osler, James Gregory Mumford, Wm. H. Welch and others of similar caliber, is indeed a privilege which is worthy of a lifetime of endeavor and effort.

REPORT OF A CASE OF ACNITIS WITH A STUDY OF THE POINT OF ORIGIN OF THE PATHOLOGICAL PROCESS.

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(*From the Dermatological Clinic of The Johns Hopkins Hospital.*)

The first description of acnitis was given by T. Fox[1] in 1878, who termed the condition Disseminated Follicular Lupus. He thought it was probably due to the simultaneous predisposition of those affected to acne and tuberculosis, but differed from acne in the following points: (1) its resemblance in color and general aspect to lupus tissue; (2) its indolent non-inflammatory course; (3) its insusceptibility to ordinary acne therapy.

In 1890 Kaposi[2] presented a case of acnitis before the Wiener Dermatologische Gesellschaft, and because of the associated vascularity suggested the name Acne teleangiectodes.

Barthélemy,[3] in 1891, was the first to describe the condition under the name Acnitis, sharply separating it from folliclis. According to him the principal differential points were its restriction to the face and the deeper location of the pathological process.

Pollitzer,[4] in 1892, believing that the disease had its origin in the sweat glands, coined the name Hydradenitis destruens suppurativa.

Crocker,[5] in 1902, showed a case before the British Dermatological Society of London. He suggested the name Acne agminata, at the same time adding that it was probably the same as Kaposi's Acne teleangiectodes. He also pointed out its resemblance to Fox's disseminated follicular lupus. The condition described by him, however, differed from these in having a more pustular aspect.

Other cases of acnitis have been described as Acne luposa, Lupus miliaris,[22] and Colloid degeneration[8] of the skin.

Pringle's[1] "A Rare Seborrhoid of the Face" and Brooke's[2] cases of "Varus Nodulosus" resemble it in many respects.

As to the pathology, most authors who have studied acnitis carefully agree as to the character of the cellular infiltration, but there is still a wide divergence of opinion as to the point of origin of the pathological process and the etiology is undetermined.

Although we can add nothing new to the latter, our researches have given such definite results as to the location of the beginning lesions that we feel justified in giving a detailed report of the following case.

The patient was a carpenter, aged 47 years. One sister had died of tuberculosis; otherwise the family history was of no importance. In 1908 the patient had had "a touch of pneumonia," and at that time had had an eruption of pimples on the back. After this he had been troubled for a short time with boils. No history could be obtained suggesting a syphilitic infection. His wife, however, had had eleven miscarriages. The children, so far as the parents know, have shown no skin blemishes. A blood test taken from the mother in 1911 was said to be "suspicious of syphilis."

The affection began, in August 1913, with the appearance of a few small nodules at the base of the nose and about the nasolabial folds, and despite treatment with potassium iodide and various salves, the process gradually extended to the forehead, chin and cheeks. There had been no subjective symptoms except a slight tenderness over the nodules when they attained a large size and became secondarily infected.

We first saw him in December, 1913, four months after the beginning of the disease. A general physical examination showed an old fibrosis of the lungs, most likely of tuberculous origin.

Scattered over the face were about 150 nodules which were grouped on the forehead, temples, base of nose, cheeks and chin [*vid.* photograph]. A few were scattered on the sides of the face, eyelids, margins of the ears and on the skin over the mastoid prominences. The scalp was free except for a small number just inside the hair margin of the forehead. The neck, trunk, extremities and mucous surfaces were not affected, and no lesions were found on any other part of the body.

The lesions varied from 1 to 10 mm. in diameter. They were for the most part discrete, although occasionally two or three of the larger nodules were confluent. They were seated on a non-inflammatory base, but in some cases, when the nodules were close together, a slight reddening and thickening of the interlying skin was present.

The lesions consisted of (1) very small nodules, barely palpable, lying at various depths in the cutis. These felt to the touch like fine shot, were freely movable on the underlying structure and the skin over them was not discolored. These early lesions could not be seen at all if viewed by direct light, but when the patient was observed from the side a slight elevation could often be seen over them. (2) Flat, slightly raised papules, varying from 1 to 2 mm. in diameter. These were of a light yellowish-brown color and in some cases were covered with a tightly adherent scale. When pressed upon with a glass slide there became apparent a central whitish opaque area surrounded by a brownish-yellow collar of "apple-jelly" tissue, which was sharply defined from the surrounding normal skin. When the scale was removed, a small opening in the center of the yellowish infiltrate was disclosed and underneath the scale one could frequently see a cheesy-like plug which had occupied the opening. This yellowish infiltrate, consisting of a gelatinous, very friable mass, could be entirely removed with a fine curette, leaving a sharply punched-out opening. This type of lesion was best observed on the forehead. On the chin and sides of the nose the nodules of this size were more elevated and cone-like in structure and were not usually covered with a scale. Here was seen, under pressure with a glass slide, a small translucent center, resembling a deep vesicle, surrounded by the jelly-like collar. Some of these nodules were pierced by a hair, in which case they resembled the ordinary pustular nodules of acne. (3) Large elevated tubercles, round or oval in shape, varying from .5 to 1 cm. in diameter. These nodules were firm and elastic to the touch or soft and fluctuating. The skin over them, depending upon the depth of the lesion, showed either a slight reddening or was of a dark red color, frequently showing a central pustulation. The softer ones contained a creamy-like, often blood-streaked material and from the firm ones could be removed the above-mentioned brownish-yellow gelatinous tissue, which was similar in every respect to the apple-jelly nodules of lupus tissue.

The blood count showed the normal cell relation. The Calmette reaction was negative, but the skin tuberculin test was positive.

The Wassermann reaction was negative in both the blood and spinal fluid. The cell count, the globulin and the gold-chloride tests for the spinal fluid were negative.

Histological Examination.—Seven nodules of various sizes were excised, fixed in formalin, and stained by the usual methods. Of this number three represented the small shot-like nodules, which were just palpable in the skin. These gave the most definite and uncomplicated picture and being the earliest lesions which could be demonstrated clinically, were studied in detail. They averaged about 1 mm. in diameter, lay in the lower half of the cutis and were sharply defined from the surrounding tissue. Their pathological structure was rather sharply separated into three parts (Fig. 2): (1) A central finely granular, homogeneous mass, containing towards its periphery a few pienotic nuclei and nuclear fragments. (2) Surrounding this a ring of cellular tissue, composed of round, oval or large spindle-shaped nuclei of the epithelioid type. These cells often lay in small groups or nests, showing a concentric arrangement. The intercellular substance in these nests had a coarsely granular, amorphous structure, but between them it was more of the connective-tissue type, showing fibrillar formation. In this layer giant cells were occasionally seen. (3) Lying between the above-described ring and the surrounding layer of normal compressed collagenous tissue were variable numbers of small round cells, in which were scattered a few swollen epithelioid cells. The nodule was devoid of blood vessels except in this outside round-cell layer. Occasionally an elastic-fiber fragment was seen in the central necrotic mass. Elastic tissue was absent from the layer of epithelioid tissue.

In the larger nodules the pathological process was not so sharply defined. Here hair follicles and sebaceous glands were involved in the expanding nodules. Groups and strands of epithelioid cells, in which many large giant cells were frequently present, alternated with masses of small round cells. The latter, however, were always thickest at the periphery of the infiltration. In one nodule showing clinically a central pustule, the center was filled with a mass of leucocytes and the picture of an acute inflammatory process was added. Mast cells and plasma cells were only occasionally seen.

One of the small nodules was cut in serial sections and a number of sections from the excised piece of tissue were mounted before the nodule was reached. It was in these

FIG. 1A.—Front View.

FIG. 1B.—Side View.

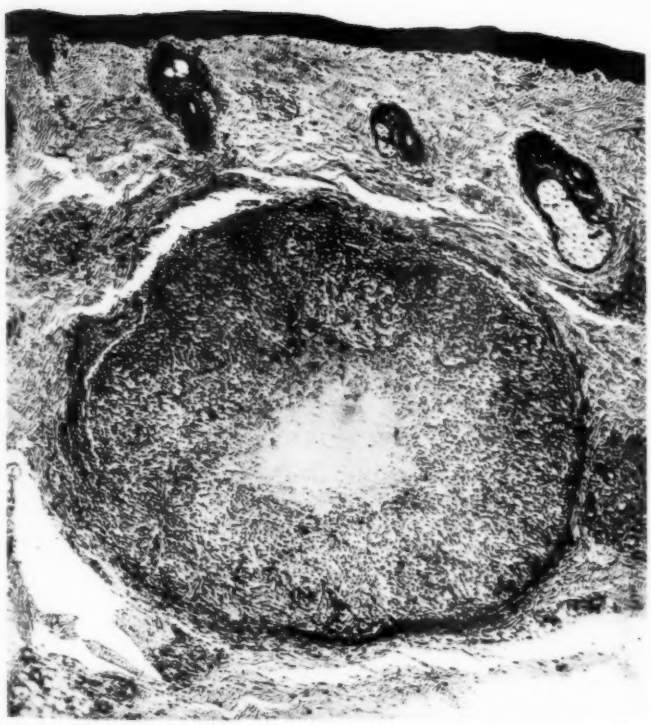

FIG. 2.—Section of one of the small shot-like lesions just palpable beneath the skin.

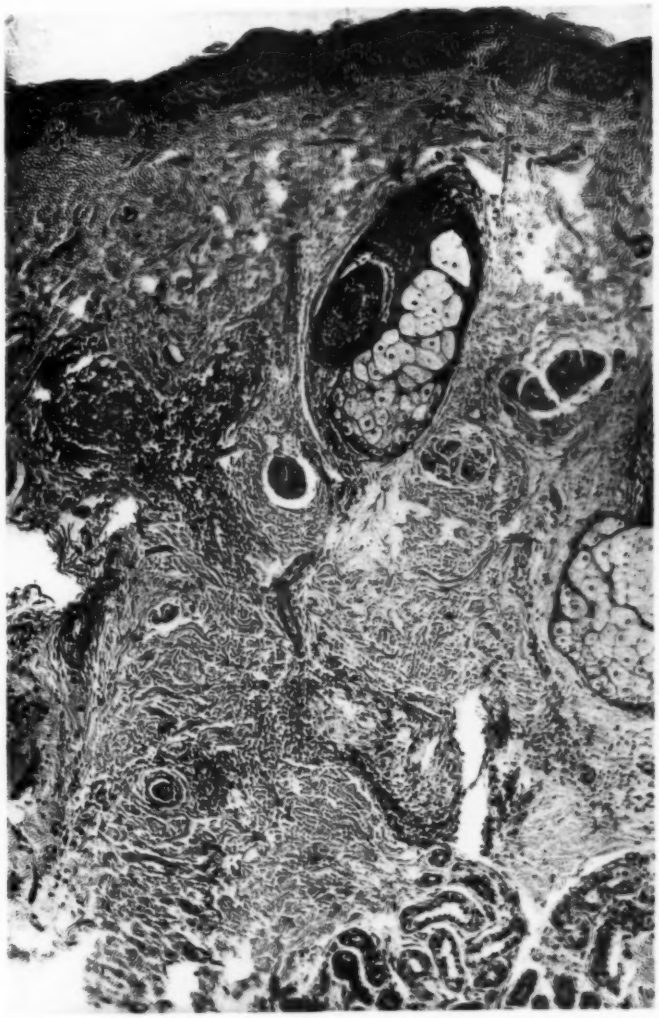

FIG. 3.—Section showing two of the beginning lesions. The upper lesion shows definitely its relation to small blood-vessels.

sections that we were fortunate enough to find three microscopical lesions which gave us the key to the point of origin of the pathological process of acnitis (Fig. 3). One of these lesions lay just beneath the epidermis, another midway in the cutis, and the third in the lower border of the cutis. They were round or oblong in shape and consisted of a small group of epithelioid cells of the same type as those described in the larger nodules. About the periphery were scattered a few small round cells and in one section a giant cell was seen. These small infiltrations could be traced throughout their entire extent in the serial sections and were in no way connected with the sweat glands, hair follicles or sebaceous glands, but lay definitely along the course of the small blood vessels. Two or more vascular branches could be traced into each nodule and in one of them red blood cells were seen lying free in the infiltrate. These branches, before reaching the nodule, became enveloped with a mantle of small round cells, which was continuous with those surrounding the nodule.

As before mentioned, there is a general consensus of opinion as to the chronic inflammatory nature of acnitis, but opinion is very much divided as to the point of origin of the pathological process. This is undoubtedly due to the fact that an insufficient amount of material, especially of the beginning lesions, has been studied. Barthélmey considers the condition a perifollicular process beginning at the base of the follicle. Its deep location differentiates it from folliclis, which has a more superficial origin. Pollitzer thought that the affection began in the sweat glands and that the giant cells and nests of epithelioid cells were products of the gland epithelium. Pernet, examining one of Crocker's cases, also found the primary changes in the sweat glands. T. Fox believed that "rete, corium and the glands were alike involved in the same morbid process, *i. e.*, the formation of lupoid tissue in their midst." Jesionek [9] found the infiltration around the hair follicles, sweat and sebaceous glands; he suggested that it may have had its origin in the blood vessels surrounding these organs. Spiegler found in Kaposi's case a young granulation tissue surrounding the hair follicles and sweat glands. Finger [10] noted a sharply circumscribed infiltration of giant cells, nests of epithelioid cells and small round cells surrounding sweat glands and hair follicles. In Shamberg's [11] cases the sweat glands were involved, but he was unable to determine whether the process had its origin in these glands or whether they were only secondarily involved.

Our studies show definitely that the primary lesion of acnitis originates in the small blood vessels lying at various depths in the cutis. The varied findings of other investigators can very well be explained by this assumption, as the concerned vessel may surround a hair follicle, sweat or sebaceous gland.

The clinical picture and the pathological microscopical findings show clearly the method of growth and the changes taking place during the development of a nodule. The process begins in the small blood vessels by the formation of a collection of epithelioid cells, which are most likely the result of a proliferation of the endothelium of the vessel and the surrounding connective tissue.

The infiltration extends peripherally, attracting to its outer zone a variable number of small round cells. If it originates in the vessels associated with the hair follicles or sweat or sebaceous glands, the picture is somewhat changed by the enclosure of these organs. Central necrosis soon takes place, owing to the absence of a blood supply in the epithelioid infiltration.

If the lesions lie very superficially and especially where the skin is taut, as on the forehead, a portion of the gelatinous ring of epithelioid tissue soon comes in contact with the overlying epithelium and necrosis is hastened in both from the resulting pressure. Drying ensues, if infection with pyogenic organisms does not take place, and the dead tissue forms the scale and necrotic plug, which is continuous with the central necrotic mass. On the cheeks and chin, where the tissues are looser, the epidermis is less frequently involved until the nodule becomes larger; then secondary infection frequently takes place, as one or more hair follicles are usually involved by the expanding nodule.

If some of the lesions having a deep origin reach a large size without secondary infection taking place, the jelly-like tissue may undergo an autolysis forming a yellowish semi-liquid material resembling pus.

Through the courtesy of Dr. Gilchrist I have studied the sections from a case of acnitis which he investigated in this clinic in 1897. The patient was a woman, aged 42, and the condition had existed for six months. It was limited to the face and the lesions resembled those of the present case, except that no pustules were present. The histological preparations from the small shot-like lesions were identical in structure with those described above. No microscopical beginning lesions could be found, as there was a very narrow margin of normal tissue in the sections.

Etiology.—The cause of acnitis is still undetermined. The resemblance of the lesions to lupus tissue has led, in most of the reported cases, to careful search for positive evidence of tuberculosis, but the results have been for the most part negative. One of Finger's patients gave a positive tuberculin test and also developed a tuberculous meningitis during treatment. The author also found, in fifty histological preparations, two bacilli resembling tubercle bacilli.

Besnier [12] obtained a positive inoculation test, but Jesionek [9] doubts his results, as the animal did not die until three months after the inoculation.

Jadassohn's [13] case gave a positive tuberculin test and inoculation of animals was successful. The patient also had a tuberculous proctitis.

Our bacteriological results were entirely unfruitful. Three guinea-pigs were injected intraperitoneally with the excised and curetted contents of the nodules. Two died within two weeks. One was destroyed by the janitor before an autopsy could be performed. The other showed only a few enlarged mesenteric lymph glands. Stained sections of one of these glands showed no evidence of tuberculosis, nor were any tubercle bacilli demonstrable. The third pig was sacrificed after three weeks time; no pathological changes were found.

Examination of a number of stained sections and smears of

the gelatinous contents of the nodules showed no tubercle bacilli; a few cocci were occasionally seen.

Cultures were made from the uninfected nodular contents on the various laboratory media, including Noguchi's spirochæte media, with entirely negative results. Cultures from the pustular lesions gave Staph. albus.

The entire gelatinous content of one of the nodules, as well as some of the nodular tissue, ground up in saline solution, was introduced into the skin of the forearm of the patient. Absorption took place completely without any definite inflammatory reaction.

Dr. Gilchrist also examined a large number of sections and smears from his case for the presence of tubercle bacilli, but was unable to demonstrate them; and the results after the inoculation of two guinea-pigs intraperitoneally were negative.

Although our results in obtaining positive bacteriological evidence of tuberculosis in the individual lesions were unfruitful, other evidence, namely, the tuberculous character of the nodules and the fact that the patient gave a positive tuberculin test, as well as showing signs of an old tuberculosis of the lungs, is very suggestive that the disease is a form of tuberculosis. Many investigators, however, Shamberg, Crocker, Barthélmey and others, are not in favor of this assumption.

Course and Treatment.—In our patient the condition seemed to have reached its height at the time of his first visit to us. Several small nodules were marked, but no definite increase in size was noticed. The patient was observed four weeks without treatment. He was then given an erythema X-ray dose on one side of the face and sulphur ointment on the other. The side treated with X-ray showed, in two weeks, a definite decrease in the size of the nodules. The portion of the face previously treated with sulphur ointment was now X-rayed, and after the slight erythema had subsided, he was given the sulphur ointment for the entire face. After an absence of about two months, when he returned to the dispensary, a very decided improvement was noticed. About two-thirds of the lesions had entirely disappeared, leaving, in some cases, especially on the hairy portion of the face, small irregular, rather deep, scars. On the temples and forehead the scars were more shallow, velvety, and slightly pigmented.

At the present time, ten months since the patient was first seen, the disease has in general subsided, but a few small freshly developed lesions are to be seen on the cheeks and eyelids.

In conclusion, I wish to thank Dr. Gilchrist, in whose department these investigations were made, for his personal interest and suggestions.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

FEBRUARY 1, 1915.

1. A Simple Method for Determining Variations in the Hydrogen Ion Concentration in the Blood. (Abstract.) Drs. L. G. Rowntree, W. McKim Marriott, and R. L. Levy.

Serum or whole blood is placed in small collodion sacs and dialyzed for five minutes against a normal saline solution. The hydrogen ion concentration of the dialysate is determined by adding a few drops of phenolsulphonephthalein and comparing the color thus obtained with that produced on adding the indicator to solutions of known hydrogen ion concentrations. A determination by this method can be carried out in a few minutes and requires only from 1 to 3 cc. of blood or serum. The results are, in general, comparable with those obtained by the use of electrometric methods.

The dialysate from normal blood (oxalated) shows a hydrogen ion concentration of from $10^{-7.6}$ to $10^{-7.8}$ and the serum dialysate varies from $10^{-7.6}$ to $10^{-7.8}$. In uncompensated acidosis, occurring in the course of diabetes, nephritis, alimentary intoxication in infants and after intravenous administration of acids to animals, the hydrogen ion concentration of the dialysate from serum was found to vary from $10^{-6.9}$ to $10^{-7.5}$. Whole blood under the same conditions gave a dialysate showing variations in the hydrogen ion concentration from $10^{-6.9}$ to $10^{-7.4}$. The intensity of the acid intoxication in these cases as evidenced clinically was, in general, proportional to the degree of departure of the hydrogen ion concentration from normal values. In all, 25 normal cases, 50 pathological cases without acidosis and 15 cases with acidosis were studied.

2. Practical Results Obtained from the Schick Reaction and the Value of Intraspinal Injections in Tetanus. Dr. W. H. Park.

FEBRUARY 15, 1915.

REPORT OF SPECIAL WORK IN THE SURGICAL DISPENSARY.

1. Plastic Surgery and Wound Healing. Dr. John Staige Davis.

On October 15, 1913, the two small rooms in the Surgical Dispensary, formerly occupied by the Social Service Department, were set aside for those patients requiring special treatment in plastic surgery and wound healing, and also for rectal diseases. Dr. Stone was placed in charge of the rectal work, and the plastic and wound healing work was assigned to me. Each clinic was held three times a week on alternating days. It has been thought advisable to make a short report and the following will show in brief the work done in plastic surgery and wound healing between October 15, 1913, and August 1, 1914:

The *total number* of patients treated was 143; of these 113 were white; 30 were colored. *Sex:* Seventy-five were males; 68 were females. *Civil State:* Fifty-eight were married; 78 were single;

7 were widowed. *Ages:* Under 10 years, 29; 10 to 20 years, 25; 20 to 30 years, 28; 30 to 40 years, 11; 40 to 50 years, 20; 50 to 60 years, 18; 60 to 70 years, 6; over 70 years, 6. Of these 13 were patients referred from the hospital; 5 were admitted to the Johns Hopkins Hospital; 6 were admitted to other hospitals in the city.

Duration of Lesion.—From half an hour in the accident cases to 30 years in some of the chronic ulcers.

Result of Treatment.—Well, 79; improved, 42; unimproved, 5; not treated, 3; admitted to hospital, etc., 14. The ultimate result of treatment of these patients admitted to the hospitals is not known.

Wassermann reactions were taken on all patients with suspicious ulcers.

SUMMARY OF CASES.

Amputation of Finger, traumatic, partial.—12 cases: White, 11; colored, 1. Males, 10; females, 2. *Ages:* Between 16 and 50 years. *Occupations:* Operator, 11; laborer, 1. *Location:* Right forefinger, 5; left forefinger, 4; left ring finger, 1; left middle finger, 2; terminal phalanx, 11; second phalanx, 1. *Duration:* One-half hour to five weeks. *Treatment:* Celluloid guard and local measures in 10 cases; well, 10. Plastic operations in 2 cases; both well.

Attempts were made to add to the length of these fingers by training the growth of granulations along a definite line by means of a celluloid tube. Better results were obtained in the instances in which the treatment was commenced shortly after the accident, as the blood-clot molded by the celluloid tube was utilized as a scaffold for the granulations. Gains of .5 to 1.25 cm. were made in the length of the fingers in 10 cases.

Anchylosis of Wrist, partial, post-operative, infected.—1 case: Admitted to hospital.

Angiomata.—17 cases: White, 17. Males, 4; females, 13. *Ages:* Between 6 weeks to 16 years. *Location:* Forehead, 4; cheek and trunk, 3 each; upper lip, lower lip, scalp, nose, face and finger, 1 each. *Duration:* Congenital, 15; three months and six months, 1 each. *Treatment:* Carbon dioxide ice, 12; well, 4; improved, 8. Excision, 4; well, 3; improved, 1. Not treated, 1.

The comparatively small number of cures in this group is due to the fact that the treatment with carbon dioxide ice requires a considerable period of time, and further applications will be necessary in several of the cases. The treatment is tedious in some instances, but the final result obtained with this agent is most satisfactory.

Contractures.—5 cases: White, 4; colored, 1. Males, 3; females, 2. *Ages:* Between 19 months and 59 years. *Location:* Fingers, 2; face, elbow and popliteal space, 1 each. *Duration:* A few months to 10 years. *Treatment:* Plastic operation and whole thickness grafts, 2; well, 1, improved, 1. Plastic operation, 1; improved. Not treated, 2. One of these patients was advised to return for operation, and one, a marantic child, is being built up for operation. There were 3 contractures following burns; 1 had followed operation with infection, and 1 operation for infection.

Deformities.—7 cases: White, 6; colored, 1. Males, 5; females, 2. *Ages:* From 2 weeks to 43 years. *Location:* Webbed fingers, 3; of these two were congenital and one had followed a burn. Finger and ear; nose and ear, 1 each, both congenital. Ear, 2; both had followed trauma. *Treatment:* Requiring operation in the hospital, 4. Plastic operation, 3. *Result:* All well.

Epulis.—1 case: Lower jaw. Admitted to the hospital.

Foreign Body.—1 case: Needle in leg. *Duration:* 6 years. Removed. *Result:* Well.

Fractures, Compound.—2 cases: White, 2. Males, 2. *Ages:* 6 and 50 years. *Location:* Left thumb, 1; left middle finger, 1. The thumb was entirely torn off, except for a narrow strip of the soft parts. *Duration:* One hour and 1 day. *Treatment:* Plastic operation on thumb. Celluloid guard on finger. *Result:* Both well, function good.

Keloid.—4 cases: White, 1; colored, 3. Males, 3; females, 1. *Ages:* Two to 38 years. *Location:* Face and chest, 2 each. Two had followed operation, and 2 had followed a burn. *Duration:* Two and a half months to several years. *Treatment:* Carbon dioxide ice, 1; improved. Admitted to the hospital, 1. Advised operation, not treated, 2.

Mole, extensive, pigmented, of chin.—1 case. Young baby. To return when the child is older. Not treated.

Papillomata.—5 cases: White, 5. Males, 3; females, 2. *Ages:* Eighteen months to 32 years. *Location:* Upper lip, chin, cheek, thumb, foot, 1 each. *Duration:* Four weeks to 10 years. *Treatment:* Carbon dioxide ice, 4. Well, 4; not treated, 1. This patient was sent to the Harriet Lane Home for a general building up.

Sinus of Neck.—1 case: The patient stopped coming before complete recovery. Operation advised, but the patient did not return. Result not known.

Tendon, Destruction of, following infection.—2 cases: White, 1; colored, 1. Male, 1; female, 1. *Ages:* 40 and 12 years. *Occupation:* Engineer, and schoolgirl. *Location:* Right forefinger, and right middle finger, 1 each. *Duration:* Two months and 5 months. *Treatment:* Plastic operation, 2; improved, 2.

Ulcer Following Burn.—13 cases: White, 7; colored, 6. *Ages:* Seven to 80 years. *Location:* Lower extremity, 7; upper extremity, 3; head, 3; trunk, 1. *Duration:* Few days to 6 years. Among these were acid burns, of leg, 2; of cheek, 1. Frost-bite and ice-bag slough, 1 each. *Treatment:* Local, 5; all well. Small deep grafts, 5; 3 well; 2 improved. Local and small deep grafts, 2; 1 well, 1 improved. Whole thickness grafts, 1; well.

Ulcer Following Infection.—9 cases: White, 7; colored, 2. Males, 6; females, 3. *Ages:* Nine to 63 years. *Location:* Lower extremity, 9. *Duration:* Few months to 30 years. *Treatment:* Local, 1; improved. Small deep grafts and local, 6; well, 3; improved, 2, unimproved, 1. Two patients did not return for treatment. Two were admitted to another hospital, and one was admitted to The Johns Hopkins Hospital.

Ulcer Following Operation.—15 cases: White, 11; colored, 4. *Ages:* Nine to 55 years. *Location:* Lower extremity, 8; upper extremity and trunk, 3 each; head, 1. *Duration:* One week to 3 months. Nine of these were house cases. *Treatment:* Local, 7; 6 well, 1 improved. Small deep grafts, 6; 1 improved, 1 unimproved.

Ulcer Following Excision of Epithelioma.—Six patients, all white. Males, 3; females, 3. *Ages:* Fifteen to 82 years. *Location:* Cheek, forehead, 2 each; scalp, finger, 1 each. *Duration:* A few days to two weeks. *Treatment:* One was grafted with Thiersch grafts; 5 were grafted with small deep grafts. All the grafts were successful, and all the patients were discharged well.

Ulcers, traumatic.—11 cases: White, 8; colored, 3. Males, 11. *Ages:* From 11 to 72 years. *Location:* Lower extremity, 6; upper extremity, 5. *Duration:* One week to 9 months. *Treatment:* Local, 5; 3 well, 2 improved. Small deep grafts and local, 6; 4 well, 1 improved, 1 unimproved. Three of these patients had been in the hospital. One was admitted to another hospital.

Ulcers, varicose.—21 cases: White, 16; colored, 5. Males, 3; females, 18. *Ages:* From 28 to 65 years. *Occupation:* Housewife, 16; laborer, and operator, 2 each; blacksmith, 1. *Location:* All were on the leg. Right leg, 5; left leg, 12; both legs, 4. *Aggravating causes:* Pregnancy, 1; typhoid, 19 years before, 1; milk-leg, 1. *Duration:* Two weeks to 25 years, off and on. Two were admitted to the hospital. *Treatment:* Local, 16; well, 8; improved, 7; unimproved, 1. Small deep grafts and local, 5; well, 4; improved, 1.

Ulcers of Leg, luetic.—6 cases: White, 3; colored, 3. Males, 1; females, 5. *Ages:* From 23 to 65 years. *Location:* Left leg, 3; right leg, 3. *Duration:* Few months to 20 years. *Treatment:* Local, 4; improved, 4. Small deep grafts, 2; 1 well; 1 unimproved. Constitutional treatment also was carried out in each case. Several patients were given salvarsan with little beneficial result. Some of the ulcers undoubtedly had originated as luetic ulcers, but had been kept open by poor circulation due to varicose veins, and secondary infection.

Varicose Veins.—1 case: Both legs. Male, 54, white. Several years' duration. Advised operation. Refused. Rubber stocking. Improved.

Warts (multiple).—1 case: Hands. Treated with carbon dioxide ice. Patient did not return for further treatment. Result unknown.

Wound, Lacerated, of Finger.—1 case: *Treatment:* local; well.

COMMENTS.

It is obviously impossible in a report of this character to give the treatment of each case in detail, so I will only mention the several methods used.

The following *operative procedures* were carried out: Curettement of ulcers; incision of edges and bases; removal of foreign bodies; excisions; tendon plastic operations; skin grafting, small deep grafts, Thiersch grafts, whole-thickness grafts; plastic operations of various kinds; applications of carbon dioxide ice.

The following *local applications* were used: *Wet Dressings.*—Gauze, wet with 1-500 aqueous solution of iodin; boric acid solution, 2 per cent; 1 per cent dahlia (basic fuchsin and methyl violet); 1 per cent basic fuchsin; 1 per cent methylene blue; 1 per cent gentian violet (methyl violet and dextrin); 48 per cent glucose solution; glycerine; olive oil; neutral paraffine oil.

Ointments.—Boric acid ointment; zinc oxide ointment; ammoniated mercury ointment; blue ointment; scarlet red, 4 and 8 per cent; amidoazotoluol, 2 per cent; azodolen, 2 per cent; pellidol, 2 per cent; dimazon, 2 per cent; balsam of Peru.

Stimulants and Disinfectants.—Tincture of iodin; nitrate of silver; pure carbolic acid.

Miscellaneous.—Old linen; rubber protective; paraffined mesh; paraffined linen; sheet celluloid.

Retentive Dressings.—Gauze and muslin bandages; stockinette; adhesive plaster.

The hot air douche was used with considerable benefit in some cases.

The treatment was often handicapped by the fact that the greater number of these patients were compelled to continue their daily occupations, and thus the most important factor, rest, was eliminated. Many of the patients have been regular in attendance and have cooperated in every possible way, but others have been most irregular in attendance, and several have not returned after the first dressing. There was no way of following up such cases, but I am glad to say that recently a social service worker has been assigned to the surgical out-patient department, who will be of great assistance in this respect.

A considerable number of these patients needed hospital treatment, especially those with chronic ulcers. There are but few beds available for such patients in this hospital, or in any other hospital. The maintenance of a ward for the scientific treatment of these cases would be a charity which would be far-reaching in its beneficial results.

New and intensive methods of treatment have been tried. The willingness of the patients to allow operative procedures in conditions heretofore treated locally, speaks for the success of the results they have seen on others.

Many of the ulcers treated were of long duration, and offered a most unfavorable field. Some of the patients had been coming to the dispensary for as long as fifteen years.

Some of these lesions have been cured, and others have been much improved. Fingers and hands have been made useful. Disfiguring angiomata have been removed.

Taking into consideration the number of years many of these patients have been coming to the dispensary for treatment, and their successful treatment in a comparatively short time by special methods, we have reason to feel encouraged. Furthermore, the economic saving to the hospital, both in time and material, to say nothing of the great benefit to the patients themselves, from the wage-earning standpoint, would seem to justify the work.

Both Dr. Stone and myself wish to thank Dr. Seem for his help in making this work possible, and the staff in the Surgical Dispensary for their cooperation.

2. Rectal Surgery in the Dispensary. DR. H. B. STONE.

In October, 1913, concurrently with the start of the work that Dr. Davis has just described, it was decided to segregate the rectal cases in the dispensary from the rest of the general surgical material. Since then Dr. Davis and myself have used the same rooms on alternating days and the two subjects have been handled in a more or less parallel manner. The new arrangements have provided more adequate conditions for the examination and treatment of rectal diseases than existed before, and it is the purpose of this paper to present the experience of the ten months of last year during which the present plan has been in operation, with a few brief comments. The material comprises a little over one hundred cases. It will be noted that very few rare conditions are included in this list and that even cancer of the rectum is not represented by a single instance. The fact that there is so much rectal work at present in a dispensary, which until now has made no attempt to encourage especially the development of this field of surgery, is rather surprising and there is every reason to believe that the volume of material from this time on should show a steady growth. One might question how feasible the treatment of these conditions in an out-patient department would be; and the purpose of this paper is to discuss this point, as well as to illustrate the economic saving to the hospital involved in the treatment as dispensary cases of many patients, who formerly were sent into the house and occupied beds for periods ranging from one to two weeks.

To make clear these points it is perhaps best to consider the individual groups of cases in order.

Abscess.—18 cases. Of these patients, only two, in whom the abscesses extended far up the bowel wall and were of considerable size, were sent into the hospital. The rest were handled without difficulty as ambulatory patients, the original operation being performed, usually with ether anesthesia, in the dispensary and the subsequent dressing being done at regular intervals thereafter. These patients complained of no great difficulty in going to and from the dispensary and in no case was there any reason to feel that the welfare of the patient was at all jeopardized by his coming back and forth.

Condylomata.—3 cases. In one case the growths were specific (condylomata lata); in the other two they were benign papillomata of the acuminate type. All of these patients were treated under ether. In the first instance the specific lesions were destroyed by means of the actual cautery. In the other two cases the tumors were excised and the bases cauterized to control hemorrhage and also to restrain any tendency to local recurrence.

Dysentery.—The one case met with was of the amebic type. The patient was sent into the hospital for treatment.

Eczema.—The one case was treated with local applications.

Fissure.—8 cases; all were very satisfactorily treated under local anesthesia. This work was first done with novocain.

Recently we have been using a mixture of novocain and quinine urea hydrochloride (1% of each). This gives a very satisfactory anesthesia which not only permits perfect freedom in the local field to be operated on, but also allows good dilatation of the sphincter. There was no class of patients more grateful than these for the relief secured by this very simple and safe surgical procedure.

Fistula.—20 cases. Several of these were of the multiple type; one or two were definitely associated with pulmonary tuberculosis. The patients showing such extensive processes were sent into the hospital, the others, who constituted a majority of all the patients seen, were operated on in the dispensary, many of them with local anesthesia. Even in those cases in which the sphincter was divided, this form of anesthesia was amply sufficient. There were no unpleasant consequences observed from sending patients home after such operations. The method of handling these cases after operation will be considered in detail later. No cases of incontinence resulted in this series of operations. In this connection I wish to express my belief that fistula is best treated by an incision radiating from the anus instead of tangential to it.

Foreign Body.—2 cases. In one case the foreign body was a fish bone; in the other a small fragment of meat bone. There was nothing of particular interest in these cases except the mechanical difficulty in dislodging the bones, which were buried in the tissues.

Hemorrhoids.—31 cases. These fall naturally into two clinical divisions, the external and internal types. All of the external type were operated upon in the dispensary under local anesthesia without difficulty and with satisfaction to the patient. In reality these cases present no greater problem than arises in the case of a small benign tumor elsewhere on the body surface. It is to be noticed that thrombotic piles should be excised, rather than incised and the clot removed. In the latter case the cavity left by the thrombus not infrequently becomes filled with clot again, giving further trouble. As to the internal cases, we have divided them into three groups according to the method of treatment best suited to the case. First, there are the very mild cases which bleed only at rare intervals and occasion very little subjective discomfort. These cases, when examined, present only moderate anatomical changes and for them a non-operative method of treatment is desirable. This consists in the use of some local application, containing sedative and astringent drugs, combined with the use of cascara or some other form of mild laxative to diminish the traumatism of defecation. Under such treatment the patient, although not cured, is certainly rendered free from any symptoms for a long period of time. The second group is made up of cases in which there are one or a few masses of localized tissue, easily accessible and definitely circumscribed. Such cases we have treated in the dispensary by removing the tumor masses under local anesthesia and securing the blood-vessels by means of catgut sutures. These patients have been allowed to go home, and in no instance so far has there been any subsequent trouble. The possibility of hemorrhage has always been borne in mind, but care is taken to secure good hemostasis at operation and growing experience is making the probability of such a complication as secondary bleeding seem remote. The last group of internal piles are those in which there is a large and extensive development of varicosites or perhaps a complete circle. These patients we have not felt justified in operating on in the dispensary, and up to the present time they have been sent into the hospital. Nevertheless, I believe that it would be entirely practical to carry out the operative treatment of these cases, as well as of numerous others, were we provided with a small 24-hour ward, where two or three beds with the necessary adjuncts could be utilized for retaining over night patients operated upon in the dispensary.

Papillæ.—This condition of hypertrophied anal papillæ, which is emphasized in many text-books as a cause of numerous rectal symptoms, has been encountered only three times, at least when it was of sufficient development for us to recognize it as a probable cause of trouble. It is dealt with under local anesthesia.

Pilonidal Sinus.—The one patient who came to us during the past year suffering from this condition, was sent into the hospital for treatment.

Poison Oak.—One case was treated with local applications.

Polyp.—There were two cases of this type, one of which was exceedingly interesting. The patient had had a growth from early childhood, which projected out of the anus for several centimeters, and had its attachment above the internal sphincter. Both of these cases afforded very satisfactory results with local anesthesia.

Proctitis.—There were two cases, both of the ulcerated type, diagnosed through the protoscope and sent into the hospital for treatment.

Prolapse.—Four cases; the patients were all sent to the hospital for treatment.

Stricture.—Two cases. In one of these the stricture was due to a thin but very firm scar following a Whitehead operation. This was divided, under ether, and forcibly dilated in the dispensary. The other case was of specific origin and presented a tubular stricture with a very small lumen about 1 cm. long. It was satisfactorily treated by repeated gradual dilatation with hard rubber dilators, in addition to the general treatment of the disease.

Ulcer (anal).—One case, probably tuberculous, was seen. This ulcer was excised under ether and the base cauterized.

Wounds.—There was one such patient treated, the injury resulting from a fall and the condition presenting no especial point of interest.

In all the cases in which operative procedures were employed, the wounded surface was packed with iodoform gauze; over this ample dressings were applied and the buttocks bound firmly together with adhesive. The patients were told to return on the third day and in the meantime were given a lead and opium pill three times a day. Upon their return the dressings were removed, the pack was displaced, the wound washed and new dressings were applied, but this time a T-bandage instead of adhesive was employed. The patient was then given cascara with directions as to the management of his dressings at home. This early start in the use of laxatives has not been followed by any disadvantage, but on the contrary seems very much better than the older custom of longer delay. In fact the absence of any severe pain when the bowels began to move has been a very noticeable feature of the post-operative history in nearly all cases.

This somewhat superficial report of the first ten months' work in this department brings forward several points that are worthy of emphasis. In the first place the provision of a room and equipment, adapted for the performance of rectal work, has considerably extended the range of material that can be treated in the dispensary and hence has increased the teaching facilities for third-year students. This teaching can be done in a much more direct and personal manner than is possible when these cases are handled in the general operating room. Further than this, the hospital is relieved of a considerable number of bed patients, who may now be satisfactorily cared for in the out-patient department. This economy and the advantage of such a change need not be dwelt on. Lastly, the possibility of improvement in managing the surgical problems, presented in this especial field, should be enhanced by the opportunity of seeing a larger amount of clinical material and possessing better facilities for handling it.

DISCUSSION.

DR. EARLE: I congratulate The Johns Hopkins Hospital in having organized in their dispensary this special branch of rectal work. A few years' experience will teach any of you, after you have taken up

general practice, just how much need there is for such instruction as you receive under Dr. Stone in the dispensary. We see over and over again in our practice the grossest ignorance of otherwise well equipped and well qualified physicians, and even surgeons, in the treatment of rectal diseases. As Dr. Stone has shown you, these cases can be treated, and are being treated at the office by those who are following this special line of work. Many patients have heretofore been confined to bed from two to three weeks for operations that could readily have been performed under local anesthesia in the office. I can only hope that you, as students, will avail yourselves of the opportunity Dr. Stone offers you for learning to deal with these cases intelligently and to discern between the gross and the minor lesions, so you will be able to treat these patients properly in your office and with as little delay from their business as is possible.

There are some things that must be especially borne in mind in rectal surgery; among them, the fact that you are always working in a field that it is almost impossible to make sterile. In these cases you have to supplement the means used in the treatment of wounds in other portions of the body with much closer supervision, remembering that one cannot close up a wound here and expect to uncover it in five or six days, with primary union, but that frequent antiseptic washes must be used and, above all things, that the bowels must not be confined too long, as was formerly the custom. It must be borne in mind that these cases should receive personal and frequent attention, and it is chiefly by such means that those who follow this line of work obtain good results.

I congratulate Dr. Stone upon his work and hope it will continue. There is great need for just such effort as his, and I am glad to see it recognized by this hospital.

3. * **A Study of the Ferments and Anti-Ferments of the Body and Their Relation to Certain Diseases.** Dr. J. W. Jobling.

THE JOHNS HOPKINS HOSPITAL HISTORICAL CLUB.

FEBRUARY 8, 1915.

1. **The Times of Vesalius. Contributions of Vesalius Other than Anatomical.** Dr. Wm. H. Welch.

It seemed a pity not to devote one of the meetings of our historical club to the celebration of the four hundredth anniversary of the birth of Vesalius. It was intended to commemorate this on a fitting scale in Belgium during the month of December when preparations had been made and interesting exercises had been arranged for in Brussels and at the University of Louvain. It is sad beyond measure to contemplate the situation which rendered it impossible to carry out that intention. However, in this country we have endeavored to do our best in the celebration of this event, exercises having been held in Boston, New York, Washington, and I believe elsewhere.

In these introductory remarks, it seems appropriate to say a few words about the times in which Vesalius lived and did his work, also of his contributions other than those to anatomy.

As you know, Vesalius was born on the last day of December, 1514, and died in 1564. This was an extremely interesting and stirring period. It was the early part of the period of the French Renaissance, the zenith of the Italian period having been reached in the preceding century, or not later than the year 1500. There were a number of events that, taken together, combined to make this one of the most stirring periods of all human history. About the middle of the fifteenth century printing had been invented, and coincident with that was the invention of cheap paper, so that the rapid spread of books, writings and knowledge was made possible. Toward the end of this century—indeed throughout its latter half and the early part of the sixteenth—came the discoveries of the great Spanish and Portuguese explorers, opening up a new world. About the middle of the sixteenth century, 1543, the very year of the publication of Vesalius' great work, the epoch-making contribution of Copernicus established the Copernican system, that theory of the solar system which was eventually to take the place of the Ptolemaic theory. Another great influence to open men's minds to new knowledge was the revival of classic learning—one of the most striking characteristics of the Renaissance. The writings of Hippocrates, of Galen and of Aristotle were made known as they actually existed and were not deformed by passing through many translations. It was not uncommon to have these writings translated from Greek into Syriac, from Syriac into Arabic, thence into Hebrew and finally into Latin before being made known to the medieval mind. It is easy to see how distorted the point of view must have been. This revival of classical knowledge brought into prominence one book of great significance for that period which had previously been very little known—the great work of Celsus on medicine.

This was also the period of great painters and sculptors, the age of Raphael, of Titian, of Michael Angelo and of Leonardo da Vinci, indeed one of the greatest periods in the world's history of art. It is interesting to note that this artistic development had great influence upon anatomy. The artists themselves were often anatomists and loved to make anatomical drawings. Leonardo da Vinci, the most varied genius probably who ever lived, a miraculous combination of art and science, apparently manifesting every capacity of the human mind, ranks as a great anatomist. The importance of his work in anatomy was hardly appreciated until his plates were studied by William Hunter in the eighteenth century. The development of art undoubtedly had a most stimulating effect on anatomical drawings and illustrations and in that way on the development of anatomy. It was surmised at one time that some of the plates in Vesalius' Fabrica had been made by Titian, but I believe this has been disproved.

This was also a marvelous period in literature, both in poetry and in prose. It is interesting to recall that one of the great names of French literature, Rabelais, was a medical man and a contemporary of Vesalius. Rabelais partly edited an edition of Hippocrates and himself dissected. He was a teacher in Montpellier, where he had also studied, and was actively identified with the profession of medicine.

As regards science, this was not the great period for natural and physical science, but rather a period of reawaking—a transitional period. The roots of the great developments of the following century are to be sought for in the sixteenth century, but the sciences of observation and the descriptive sciences like anatomy, botany, zoology, and to some extent geology and mineralogy, all had notable development at this time. Leonardo da Vinci was one of the greatest figures in the development of geology.

In botany it was the fascinating time known as the age of the herbalists, a collection of whose works forms a most interesting task for the book lover. The herbalists had great influence on anatomy. Indeed most of them were physicians.

Modern zoology dates from Gessner and Aldrovandi. Gessner was a contemporary of Vesalius and was a great botanist as well as a great zoologist. His botanical works were not published until much later, but his zoological works appeared during the sixteenth century.

With regard to medicine, this was also an interesting age. We think of the humanists in medical history as a particularly characteristic and charming type. They were good physicians and among them there is no better example than our English hero, Thomas Linacre, who founded the Royal College of Physicians in the reign of Henry VIII. The medical humanists were characterized by love of classical learning, and often believed that the

* To be published later in the Bulletin.

salvation of medicine rested on going back to the writings of Hippocrates, of Galen and of Celsus.

This was a time also when certain diseases either became known or else were accurately studied for the first time, and we find something approaching a good portrayal of disease based on accurate observation. That, of course, was not the dominant note, but this characteristic may be picked out in the writings of certain physicians. A good example is the monograph of John Caius, the founder of Caius College, on the sweating sickness. About the end of the fifteenth century syphilis began to spread with appalling severity, and the study of this disease was taken up by a number of physicians. It was found to be quite irreconcilable in its interpretation, and especially in treatment, with the prevailing Galenic doctrines of pathology. The study of these epidemics, then, marked a certain attack upon the authority of Galen.

The three great names of the sixteenth century in medicine are those of Vesalius, Paracelsus and Ambroise Paré, all others being more or less overshadowed by them. There are other interesting names also, as we pathological anatomists like to recall. That of Frascatorius, for instance, who is one of the most fascinating of figures. I do not believe justice has been done to him yet. He lived in the humanist circle in Florence and also in Padua. He was a poet and wrote on a subject that would hardly be conceived as admitting of real excellence—syphilis—but the work is conceded to have actual poetical merit, besides being historically important from the fact that we date the name syphilis from this poem.

As I said before, Paracelsus was one of the greatest figures of this period—that iconoclastic genius, typical perhaps of the German Reformation, who is sometimes spoken of as the Luther of medicine, and who was the enemy of Galen, Aristotle, in fact of all authority. The Germans give him, I think, a degree of influence which others are not inclined to allow, and he was indeed a remarkable character.

Ambroise Paré is another of the great figures. He is identified with the history of surgery. The life of Paré is a fascinating study in many ways. It is interesting to remember that his is one of the well known names in French literature. In books of French prose of the sixteenth century, you will find that Paré figures as one of the writers of terse, vigorous prose at a time when French prose was being established as an adequate medium of expression.

However, our main interest lies with Vesalius. He was born in the city of Brussels, and was of German ancestry. His father was Court Apothecary to Charles V, and it is evident that the family had some influence. Vesalius received his education in classical studies at the University of Louvain. This was the usual education of the day—Latin, Greek and mathematics. That which has come to be known as our modern system of liberal studies was practically worked out at this period of the Renaissance. Louvain was not noted as a university for humanistic studies. Indeed Erasmus, who was there at this time, felt much more at home in Holland, or in Bâle.

In about his eighteenth year, Vesalius went to Paris for his medical education. Here he was the pupil of Jacobus Sylvius. Other teachers at that time were Jean Guinter Andernac and Fernel. At Paris, Vesalius was a fellow pupil of Servetus, the discoverer of the lesser circulation from the right to the left heart. Vesalius pictures this period of his studies at Paris as lamentably deficient. He describes his teacher, Jacobus Sylvius, in a most unattractive light and says that his opportunities for study were poor indeed. The picture that Vesalius gave of Sylvius is the traditional one, although I believe there is some reason to think that it may have been overdrawn. When Vesalius had been in Paris for about three years, the war between Francis I and Charles V broke out, in consequence of which Vesalius returned to Louvain, where he remained for about a year. He also served for a few months in the army of Charles V.

About 1537 Vesalius reached Venice and the next six years form the most productive period of his life. The university belonging to the Republic of Venice was at Padua, where the spirit was probably freer than that in any other part of Italy. After having been appointed to make public dissections at the University of Padua, Vesalius was made professor of surgery, including anatomy. John Caius was a pupil of Vesalius at this time. Another interesting contemporary, although a little later, was Montanus, who taught medicine by bedside instruction. The history of clinical teaching dates from this period at Padua. It was during these years that Vesalius prepared his great work, the Fabrica, which was published in 1543. Before this he had published another work, the Paraphrases of the Ninth Book of Rhazes, which was practically an inaugural dissertation. Vesalius received the degree of M. D. in Padua, although he had previously received it in Bâle. This first publication of Vesalius was a type of work very common in those days, being partly a translation and partly a commentary. For his work he selected the most interesting book of Rhazes, that relating to the treatment of disease. This appeared in 1537. It was in 1539, I think, that Vesalius published a little work entitled An Epistle on the Selection of the Vein to be Bled. It is interesting from the fact that he took part in a discussion of that century between the Arabists and the Galenists, or the anti-Arabists. The doctrine of the Arabists was that known as revulsion, which claimed that in bleeding, especially in pleurisy (probably what we would now call pneumonia) the patient should not be bled on the side where the pain was felt, whereas Hippocrates had taught that one should bleed on the side of the disease, or on the side of the pain. This may seem but a trifling matter, but it shook the entire continent. Popes were appealed to, Charles V was asked to give his judgment—indeed it is one of the most interesting examples of the state of mind of medical men of the period in their attitude toward the writings of the Arabist physicians and in their going back to Hippocrates. Vesalius was against revulsion.

The dedication of the Fabrica to Charles V was written in 1542 and Vesalius went to Bâle to superintend the publication by the firm of Herpst, one of the publishers of the day. The printers in those days were wonderful men and scholars of the highest rank. Among them were the Aldines in Venice, one of them a great anatomist also. It is known that Erasmus went to live in Bâle because of the publishing firms there. Vesalius' Epitome, nowadays an extremely rare volume, appeared in 1543.

From the time that Vesalius secured his leave of absence to go to Bâle, a most extraordinary change took place in his life. He was at that time in his twenty-ninth or thirtieth year, which marked the end of his career as a productive worker. When he went back to Padua his work had been published. It produced a great sensation, because the essental characteristic of his attitude is his correction of the errors of Galen, based upon actual observation of human dissections. Vesalius really made modern anatomy. It has gone on developing continuously from that period. Indeed he gave it a prominence in the medical curriculum which it is only just beginning to lose. For years it was the only subject the students came into contact with directly by observation, and so it had an educational value that no other subject could have.

The publication of the Fabrica, as I said, raised a storm. Vesalius' own teacher, Jacobus Sylvius, published a scandalous attack upon him. That is where Sylvius did himself great harm. One of Vesalius' pupils, Columbo, was a great antagonist and apparently an intriguer. When Vesalius returned to Padua, he found the situation exceedingly unpleasant and became greatly discouraged; it is not apparent why he could not have gone on lecturing, but

he was greatly disheartened and burned his manuscripts. His career practically ended here, although he lived until 1564. He afterwards became Court Physician to Charles V and had a lucrative and probably fashionable practice, but his life as a man of science was over, all of his work having been done before he was 30 years of age. A most excellent description of Vesalius is to be found in a volume by Sir Michael Foster, Lectures on the History of Physiology. It is supposed that a very attractive offer from the emperor may have had something to do with Vesalius' withdrawal from his chair at Padua. After this, his most interesting publication was the one on the China root, with which he treated the emperor. The book contains a great deal of personal matter for the biographer of Vesalius and makes interesting reading of the times.

In 1563 Vesalius started on a pilgrimage to Jerusalem, no one knows exactly why. The most common theory is that in making a post-mortem examination and opening the chest, the heart was found beating. In other words he was doing a vivisection, supposing he was making a post-mortem. It is said he was brought before the Inquisition and that, the emperor having used his influence, he was told if he would go on a pilgrimage the proceedings would be stopped. Another explanation is that his domestic life was exceedingly unhappy and he seized an opportunity to escape. Still another version has it that his court life had become wearisome to him. At any rate he started out on this so-called expiatory pilgrimage. He went to Venice first and there received an offer to come back to his old chair at Padua, which he agreed to do on the completion of his voyage. On his way to Jerusalem he was shipwrecked, however, and died on the Island of Zante.

Sir Michael Foster in the first chapter of his Lectures on the History of Physiology during the Sixteenth, Seventeenth and Eighteenth Centuries, speaks of Vesalius more than once as the founder of physiology, by which he means the founder in the sense that a knowledge of structure is essential for the development of physiology. It is not meant in the sense that he made important contributions to our knowledge of the activities and functions of organs. Of course with that conception, Vesalius' work was epoch-making for physiology, just as it was for medicine in general. Vesalius was essentially Galenic in his physiology. This is what he says of the central point in the Galenic doctrine of the physiology of the circulation. In that doctrine the blood is made to pass from the right ventricle to the left ventricle through invisible pores in the septum between the ventricles. Vesalius says:

"The septum of the ventricles, composed as I have said of the thickest substance of the heart, abounds on both sides with little pits impressed in it. Of these pits, none, so far at least as can be perceived by the senses, penetrate through from the right into the left ventricle, so that we are driven to wonder at the handiwork of the Almighty, by means of which the blood sweats from the right into the left ventricle through passages which escape human vision."

This is interpreted usually as unintentional sarcasm, but Vesalius has nothing to substitute for the view of Galen. However, he tells us in a later writing that "he accommodated his statements to the dogmas of Galen," not because he thought that "these were in all cases consonant with truth but because in such a new great work he hesitated to lay down his opinions and did not dare to swerve a nail's breadth from the doctrines of the Prince of Medicine."

We owe to Foster the credit for calling attention to certain contributions of Vesalius to physiology. He writes as follows:

"That physiological problems were before his mind, that he had thought over, and indeed had tried to solve them by experimental methods is shewn in the brief chapter 'Some Remarks on the Vivisection of Animals,' which is the last chapter in his great work. In this he relates his experiments on muscle and nerve, shewing that that which passes along a nerve in order to bring about movement passes by the substance and not by the sheath of the nerves. He tells us that it is through the spinal cord that the brain acts on the trunk and limbs, that an animal can live after its spleen has been removed, that the lungs shrink when the chest is punctured, that the voice is lost when the recurrent laryngeal nerve is cut, that by artificial respiration an animal can be kept alive though its chest is laid wholly bare, and that under these circumstances a heart which has almost stopped beating may be revived by the timely use of the bellows.

"Obviously his vigorous and active young mind was starting many inquiries of a purely physiological kind, and he was aware that much of the physiology which he had put into his book would not stand the test of future research. He knew more particularly that the chapter in that book in which he treated of the use of the heart and its parts was as he says 'full of paradoxes.' But he was no less aware that his bold attempt to expound the plain visible facts of anatomy was of itself enough to raise a storm of opposition; he feared to jeopardize his success in that great effort by taking upon himself further burdens."

You will observe that Sir Michael Foster attributes to Vesalius' Galenic explanations in describing the structures to the fact that he did not wish to jeopardize the success of his great work by any deviation from more or less canonical authority. Foster also comments on the fact that Vesalius was ahead of Descartes in the idea that the mental activities were a product of the brain.

Another very interesting side of Vesalius is that he was an anthropologist. He was much interested in the shape and character of the skull and noted in his examinations the flattening of the occiput which he regarded as characteristic of the German race. The type of Germans he examined, however, probably belonged to the Alpine race.

2. The Relation of Vesalius to Anatomy and Anatomical Illustration. (Illustrated.) Dr. Frank Baker.

Andrew Wesel, better known to us by his Latinized name Andreas Vesalius, was born in Brussels on New Year's morning 400 years ago. The main facts of his career are well known: how after a preliminary course at Louvain he studied anatomy in Paris under Jacobus Sylvius and Günther von Andernach, returned to Louvain, and afterward went to Padua where he was appointed professor of surgery when only 22 years old, and conducted public anatomical demonstrations both there and at Bologna, and at 28 years of age, published that stupendous, monumental work, the Humani Corporis Fabrica.

When a mere boy he dissected mice, moles, rats, cats, and dogs, and it was probably by this means that he acquired that skill of manipulation that enabled him to demonstrate so rapidly in public where, contrary to the usual practice of the time, he always performed the work himself.

The Fabrica is a work remarkable not only for its text but also for its illustrations which are totally different from anything previously seen, as they delineate the structures accurately and naturally. Previous illustrators contented themselves with diagrammatic figures of an almost childish character showing details often supposititious, while in the Fabrica we have a pronounced artistic method and a treatment so forcible, robust and true that the work has been ascribed to Titian and other great artists of the period. The illustrations are now generally thought to have been done by Jan Stephan van Calcar, a Flemish pupil of Titian, but there are strong reasons for supposing that they were largely the work of Vesalius himself. It is known that he could draw, as his first publication, a commentary on a pharmacological book, was illustrated by drawings of plants; in his public lectures he used large drawings to show relations of organs not yet exposed, and he was accustomed to mark on the cadaver the outlines of the

bones and the joints. Throughout the Fabrica he nowhere mentions van Calcar, and moreover the illustrations could only be made by a person perfectly familiar with the anatomy of the parts shown. Skill in drawing is not infrequent among anatomists. Just prior to the time of Vesalius the great artists of Italy, Leonardo da Vinci, Michael Angelo, Raphael and others dissected the human body to perfect their knowledge of exterior form and of action. Leonardo's drawings of his dissections are so accurate that it has been alleged that Vesalius plagiarized from them. Such a charge is evidently untenable, as those drawings were carefully concealed and have only recently been published. Their very legends are so written as to be intelligible only to the initiate.

In the text of the Fabrica we have the first adequate description of the structure of the body based upon actual observation. It has sometimes been asked what did Vesalius discover, since no organs of note were named for him. It may be said that in a sense he discovered the correct gross anatomy of the entire body, as there is no region that he did not illuminate by his observations. A few of the structures not previously mentioned by others, yet described by him, are the internal pterygoid and lingualis muscles, the inferior longitudinal sinus, the septum lucidum, the seminiferous ducts. Considering that he had not the aid of the microscope, it is remarkable how just an idea he obtained of the intimate structure of the liver, the kidney and the spleen. He did not trouble himself much with speculation, being content to record his own observations. In theory he was a Galenist. While corrections of Galen swarm on almost every page he evidently holds by the doctrine of the "spirits," though he does declare that the nerves are not hollow tubes.

It is not surprising that in such a herculean task as he performed he made some errors. He thought there was a fibrocartilage in the shoulder joint, that the spleen emptied a secretion into the stomach by the vasa brevia of the splenic artery, that the crystalline lens was in the middle of the eyeball, that the olfactory nerve conveyed air to the brain. Some of his errors were corrected during his lifetime by Fallopius and Eustachius.

You are aware of the tremendous controversy that the publication of the Fabrica raised, and that Vesalius, angered at the injustice shown him, shortly after publishing a second edition of the Fabrica, burned his manuscripts and retired to the Spanish court. He was proud, sensitive, impatient of opposition, indignant at abuse. He says in the letter on the China root, written in 1546, that he had been advised to moderate his attacks on Galen, but he cannot lie about what he has himself seen. It is the equivalent of Luther's "Ich kann nichts anders."

We know but little of the secret reasons that may have led him to abandon his work in the midst of what seems to us now a brilliant success. It is often alleged that it was the result of machinations of the theologians of the time. It was undoubtedly a great loss to science, for he was a pathmaker and proclaimer of truth, one who brought science back to rational observation. He was one of those who work—

> "Each for the joy of the working, while each, in his separate star,
> Shall draw the thing as he sees it, for the God of things as they are."

(Dr. Baker exhibited numerous lantern slides, showing cuts from the Fabrica, the great contrast between them and previous work and the influence they had on subsequent anatomical illustration. The anatomical drawings of Leonardo were also shown, and contrasted with the work of Vesalius.)

3. The Personality of Vesalius. DR. F. H. GARRISON.

Dr. Welch, in his inimitable, contrapuntal way, has shown the relation of Vesalius to all the cultural phases of the Renaissance period. Dr. Baker has made us see, from the actual illustrations, how great a work the Fabrica is, and how Vesalius made anatomy a subject of equal importance with painting, sculpture, or any other branch of art or science. With the aid of Dr. Harvey Cushing's remarkable series of Vesalian portraits, which includes a number of paintings not listed by Roth, I hope to give some impression of the kind of man Vesalius was, using a few other pictures I have ventured to add to those which Dr. Cushing has kindly lent me. As we pass these Vesalian portraits in review, let us reflect that this great physician was not only the man who put scientific anatomy on its feet, and made it viable and respectable, but was, in his fiery youth, one of the protagonists of free thought, one of those to whom we owe such moral, intellectual and spiritual liberty as we have. He stood for the truth in science, that the truth, as he saw it, should be spoken.

Beginning with the wood engraving in the first imprint of the Fabrica (1543), we see a stocky burly figure, evidently of short stature, with shaggy hair and beard, a tip-tilted nose, suggesting native pugnacity and a satirical disposition, obviously a man full of pluck and courage; also a man of strife and contention, not given to brooking opposition, and inclined to make himself disagreeable to those who opposed him. "Hardly the sort of man," Dr. Fletcher used to say, "that one would care to have an argument with." The expression of the eyes in the Fabrica engraving is unprepossessing, as we shall see by comparison with the oil portraits. One point in this engraving is of special importance. We see Vesalius with an ink pot and manuscript before him, holding a dissected forearm, evidently engaged in jotting down his findings. This, with the splendid title-page of the Fabrica, tells us how much he respected his calling, that he was not above his business, no snob, in spite of his well-to-do origin, and that he used his strong personality and his social position to make his subject respected and honored by all men. Passing now to the Glasgow portrait by Calcar, which was once owned by William Hunter, we have the same pugnacious turned-up nose, and the combative, not very reassuring expression of the eyes, which are, however, uniformly dark, striking and expressive in these oil portraits, an expression which somehow indicates a disharmony, as of a not entirely happy man, with nothing of the serenity and repose which we see in such faces as those of Lister, Trousseau and Carl Ludwig, or in such anatomists as Sir Charles Bell and Henle, who were fascinating through their artistic talents, or Hyrtl and Oliver Wendell Holmes, who were beloved for native kindliness, ready wit and good humor. In all the other portraits in Dr. Cushing's series, which I hope he will some day describe at length, there is a certain resemblance. The eyes in all these pictures remind us of Scotch faces we have seen, suggesting tenacity of purpose, readiness for argument, perhaps an excess of devotion to the intellectual side of things. These oil portraits indicate Vesalius' sense of his superior social position, that he was no mere scrub, to be thrust aside and trampled upon, but a man of the world, who had played his part in the larger life, "used to something," accustomed to have his own way and inclined to let people give the wall to his peculiarities. One who, as Dr. Cushing has said, was not the least bit afraid, a hard hitter, every inch of him a man. We can read these traits clearly, because these courageous, straightforward characters are inevitably open and above board, have nothing to hide, are not subtle or inscrutable. The defects of their qualities are that they are not clever, not gracious, not always considerate of others, and hence, since "the world an ancient murderer is," are in a way to set traps for their own undoing. The only fault which has been imputed against Vesalius is that, in 1544, he gave up his life-work, burned his manuscripts and became Court Physician to Charles V, perhaps in order to place himself beyond the reach of Sylvius, Columbus, and his other enemies, who would gladly have seen him haled before the Inquisition. At any rate, Servetus was burned in 1553,

and we cannot blame Vesalius if (his common sense coming to his aid), he said, "environment wins," and became suddenly worldly wise. But at what a cost! To live as a hanger-on of courts, sacrificing the work which was the very bread and wine of his mind and giving himself up to that complacency of creature comforts, the imputation of that worship of wealth, power and worldly place, in and for themselves, which is esteemed profoundly middle-class. In 1561, the old spirit is set aflame by the publication of the Anatomical Observations of Fallopius, and then—the pilgrimage to Zante and the end.

In Dr. Cushing's series of paintings of individuals resembling Vesalius, the Tintoretto in the Pinakothek (Munich), supposed to be Vesal, the portrait from the Louvre, and the Moro from the National Gallery (London), have all some points of resemblance. The portrait of a sculptor by the Venetian painter, Moroni, may be said to epitomize the Vesalian type of countenance, as seen in the Fabrica engraving. There is the same shaggy strength and sturdiness and the suggestion that the individual might be a dangerous one to cross. The Goya portrait, which I have ventured to add, representing General Juan Martin, surnamed "El Empecinado," a Spanish *conquistador*, possibly a cut-throat, like Sparafucile in "Rigoletto," may be said to suggest the Vesalian type of head with all the elements of good left out of it. A photograph of G. F. Fitzgerald, an eminent mathematical physicist of the Ulster school, who, like Vesalius gave up his life-work, but for the definite purpose of advancing the cause of education in Ireland, represents a face full of soul and fire. There is a similar expression in certain pictures of the anatomist Joseph Leidy, and we might imagine the countenance of Vesalius lighted up in the same way, when stirred by enthusiasm for his work. The Whistler portrait of Carlyle, a head which is Vesalian in contour, has some of the elliptical tendencies of the Impressionist School. There are gaps and blanks in the face and it is of this painting that a critic has said that the artist "has not told us one significant fact about his model, his nationality, his temperament, his rank, his manner of life." [Here a series of lantern-slides was introduced, representing women of different races—Italian, Spanish, Jewish, Servian, English, Irish, Scottish—each of highly specialized type, assimilating to a certain norm of facial beauty set by Titian. All are more or less alike, yet it would not be difficult to point out the differential characters of race in each; but nothing special could be predicated of the character, temperament or morale of the individuals represented because the type is ambigous or undecipherable, appeals more to our sense of beauty than to our sense of character.] In the faces of men of letters and science, of rugged characteristics, whose lives have been as an open book, it is not so difficult to read some of their traits. In Carlyle, the resemblance to Vesalius is precisely in the contour of the head, particularly in the jutting, crag-like forehead and the short, blunt, obstinate nose of the Scotch country people. The photograph of 1860 gives us the Carlyle of tradition, gloomy, scornful, dyspeptic, unhappy, suggesting the memorable sentence in his diary: "The ground of my existence is as black as death."

All this is very unlike Vesalius, of the *grande bourgeoisie*, courted and honored by the great, yet with all of Carlyle's contrariness and whimsicality, there is, you will admit, a resemblance, in that the resolute, aggressive Vesalius, like Carlyle, stood out staunchly for his own subject, taught all the world of his time that scientific anatomy, like poetry, painting, sculpture, music, mathematics, physics, or the other fundamental branches of science, is a big subject, is, as Dr. Welch has said, the "foundation stone of scientific medicine."

In the dark eyes of Beethoven, as seen in Hornemann's miniature of 1802, there is a resemblance to some of the portraits of Dr. Cushing's collection, particularly in the extraordinary dilatation of the pupil, upon which all biographers of Beethoven dwell. Beethoven, too, had the highest respect for his calling, in fact, was, with Händel, the first to make the musician and the composer respected in society.

What has all this to do with the personality of Vesalius? Well, first and foremost, Vesalius, a native of Brussels, his genius of the Germanic order, with the wonderful power of assimilating and coordinating knowledge, was, in every sense of the world, a cosmopolitan, a man of the world and a citizen of the world. While he does not belong to the sacred band of "prophets, transfigured saints and martyrs brave," like Servetus or More or Bruno or Lavoisier or Semmelweis, he had, in his ardent youth, something of the spirit of those who risk "their lives, their fortunes and their sacred honor" for the cause of truth, something of the Huxley type; in character, something of these blameless honorable lives. But he is of chief interest to us in that he used his commanding position to make anatomy a world subject like art or poetry or philosophy. We might define the Fabrica as a world anatomy, in the same sense that the Iliad, the Divina Commedia, Hamlet and Faust are world poems, or Beethoven's symphonies are world music. Byron and Walter Scott were hasty, careless writers, poor stylists, like Vesalius, yet they too took all Europe by storm as romantic poets and novelists, and for the same reason, namely that their work was not narrowly racial, national and local, but had in it elements which appeal to and are common to all mankind. And so, to borrow Lord Morley's eloquent words about Byron, the judgment of mankind, the *Securus judicat orbis terrarum*, has agreed to place Vesalius in "that band of far-shining men of whom Pericles declared the whole world to be the tomb."

List of Works of Vesalius Exhibited.

From the Surgeon General's Library (courtesy of Dr. F. H. Garrison):

Paraphrasis in nonum librum Rhazae, ad regem Almansorem de affectuum singularium corporis partium curatione. 10 p. l., 224 pp., 4 l., 16mo. (R. Winter, 1537.)

Epistola, rationem modumque propinandi radicis Chynae decocti . . . . pertractens: et praeter alia quaedam, epistolae cuiusdam ad Jacobum Sylvium sententiam recensens, veritatis ac potissimum humanae fabricae studiosis perutilem; quum qui hactenus in illa nimium Galeno creditum sit facile commonstret. 204 pp., 7 l., fol. (Basilae, ex officina Joannis Oporini, 1546.) Bound with Dantz (J) Universales Joannis Mesue canones. fol. (Basilae, 1545.)

From the library of Dr. Henry Barton Jacobs:

Andreae Vesalii Invictissimi Caroli V. Imperatoris Medici Opera Omnia Anatomica & Chirurgica. Cura Hermanni Boerhaave Medicinae, Botanices, Collegii Practici, & Chemiae in Academia Lugduno-Batava Professoris, & Bernhardi Siegfried Albini Anatomes & Chirurgiae in eadem Academia Professoris. Tomus Primus et Secundus. (Lugduni Batavorum. Joannem du Vivie et Joan & Herm. Verbeek, MDCCXXV.)

From the Howard A. Kelly Collection of The Johns Hopkins Hospital Library:

Andreae Vesalii Bruxellensis, scholae medicorum Patuinae professoris, de Humani corporis fabrica. 7 l., 663 pp. (Basileae, Joannis Oporini, 1543.)

Von des menschen cörpers Anatomey, ein kurzer, aber vastnützer ausszug, auss D. Andree Vesalij von Brussel bücheren, von ihm selbs in Latein beschriben, unnd durch D. Albanum Torinum verdolmerscht. fol. (Basel, Johann Herpst, 1544.)

De Humani corporis fabrica. Epitome: cum annotationibus Nicolai Fontani, Amstelredamsis medici. fol., 112 pp. (Amstelodami, apud Joannem Janssonum, 1642.)

Epistola, rationem modumque, propinandi radicis Chynae decocti . . . . pertractens: et praeter alia quaedem, epistolae cuiusdam ad Jacobum Sylvium sententiam recensens, veritatis ac potissimum humanae fabricae studiosis perutilem; quum qui hactenus in illa nimium Galeno credituum sit facile commonstret. 16mo. 100 pp. (Venetiis, 1546.)

THE LAENNEC.

FEBRUARY 24, 1915.

1. * **Early Diagnosis of Pulmonary Tuberculosis.** DR. L. HAMMAN.
2. * **The Results of Inducing Pneumothorax in Pulmonary Tuberculosis.** DR. M. F. SLOANE.
3. * **The Occurrence of Tubercle Bacilli in the Circulating Blood.** DR. C. R. AUSTRIAN.
4. * **Results of Sanatorium Treatment.** DR. S. WOLMAN.

* To appear later in the BULLETIN.

NOTES ON NEW BOOKS.

Skin Diseases in General Practice. By HOLDIN DAVIS. (*London: Henry Frowde and Hodder & Stoughton, 1913.*)

The chief reason the author gives for publishing this book is that so few text-books on the subject are sufficiently practical for general use. It is undoubtedly true that the arrangement of most text-books presupposes some knowledge of skin diseases, and that no practical method is given for making diagnoses, although some works on dermatology have tried to correct the latter fault by introducing a chapter on regional distribution, in which are listed the diseases that attack any given locality.

This work by Dr. Davis is simply an elaboration of this scheme. But although this is truly a step in the right direction, many difficulties must be overcome before such an arrangement can be considered ideal. That there must be endless repetition the author quickly discovered, and endeavored to correct by describing, according to the older method which he decried, three groups of diseases, viz.: those due to pyogenic cocci, eczema and syphilis. After these come the chapters on the diseases attacking various regions. While one can appreciate the reasons for describing eczema and syphilis separately, there are other diseases that, from their arrangement, distribution, etc., present more difficulties in the way of diagnosis than those due to pyogenic cocci.

To make such a classification as this most practical, there must be added other descriptive details, and it is probable that it would enhance the value of such a scheme if, instead of merely listing the various diseases, they should be grouped according to their chief objective symptom, whether erythematous, papular, vesicular, pustular, scaly or crushed.

The book is written in a conversational manner, which makes it decidedly attractive. The descriptions of the various diseases are accurate and sufficiently complete, though we must take exception to the statements that impetigo never occurs as a solitary lesion, and that it is the commonest skin disease. One also notices a number of anomalous arrangements, such as grouping both forms of sycosis under furunculosis; calling a dermatitis due to external irritants dermatitis traumatica; describing dysidrosis under eczema; grouping lichen planus with erythema multiforme, urticaria, etc., as an eruption of toxic origin; calling lichen chronica simplex a circumscribed prurigo, and others.

Treatment is described in a simple but satisfactory manner and a special chapter is given to "Some Modern Methods of Treatment."

The illustrations are fairly numerous and well selected, but not very clear.

Infection and Resistance. By HANS ZINSSER. $3.50. (*New York: Macmillan Company, 1914.*)

An admirable book—a treatise the equal of any of its kind. The author has treated a complex and technical subject with such clarity and in so charming a manner that the labyrinthine reasonings of this branch of medical science seem easy and direct.

In developing each of the topics dealt with, the author carries the reader through the evolution of knowledge of the subject in hand; the steps needed for the solution of problems are indicated, the researches that led to the finding of these solutions abstracted and the conclusions arrived at detailed. Where discussions have arisen the two or more aspects of the controversy are presented and the authority for the several views is quoted. The knowledge of the more recently studied phases of immunity is carefully analysed and judiciously set forth. This is especially true of the chapters on anaphylaxis and vaccine therapy.

From the happy choice of the title through the excellent chapter on Colloids, by Dr. Stewart Young, one is favorably impressed with the book. It is a work that satisfies a need, for it places in the hands of those interested a clear, comprehensive, critical and authoritative digest of a most important subject. The bibliography is extensive, the index ample, and except for a few minor typographical errors, such as the misplacing of a decimal point in several of the tables (pages 107, 207), the use of "titrated" for citrated, on page 442, and a few equally trivial mistakes, no criticisms seem in order.

Poverty and Tuberculosis: The Home Hospital Experiment, 1912-14. Published by the New York Association for Improving the Condition of the Poor, 105 E. 22d street, New York City. Publication No. 84.

This booklet contains the result of two years of the Home Hospital experiment, and the work done demonstrates three things:

1. It is possible to treat families in which one or more members are afflicted with tuberculosis, by keeping the family together, in their own individual home, without danger to other members of the family.

2. The results of training patients in their own homes under satisfactory conditions of living, with adequate medical supervision, compare favorably with results secured by removing the patient from his home and treating him in a sanatorium or other special institution for tuberculosis.

3. In the case of a family in which there are combined tuberculosis and poverty, care of the family as a unit by the Home Hospital method costs less than to break up the family, as is done under other methods of treating families with tuberculosis.

Modern methods of treatment recognize the psychological factor in the care of all patients and especially so in those suffering from tuberculosis. Take a man or woman away from home and family, and there is then the worry about the family added to that incidental to the disease. But if the treatment can be carried on at home, the mental attitude, rather than retarding, aids in the cure.

The Home Hospital is a large, clean apartment house, each apartment consisting of from two to four rooms, and provided with a sleeping porch. A roof garden has a solarium for patients "taking the cure." The general scheme of the building is to provide the maximum amount of fresh air and sunlight. In this building are over two hundred individuals, 130 of whom are patients, this being one-half as many patients as are in the New York or Presby-

terian Hospital. The average number of patients is greater than at the Trudeau Sanatorium at Saranac Lake, N. Y.

The Home Hospital idea is that of a decently constructed house, with a decent budget available to provide adequate nourishment, together with provision for constant medical and nursing supervision of the family; and it would seem that, given these, the spread of tuberculosis can practically be prevented.

The reader will be impressed with the fact that the Home Hospital is treating not only tuberculosis, but all cases of sickness occurring in the families, and advising them in hygiene, so that the resistance of all the individuals may be raised and thus sickness be prevented.

Furthermore, the supervision is more than medical; it is moral also.

The paper is exceedingly interesting. This is the first experiment along such lines; the work has been done systematically and careful records have been made. The results are appended in tables and the whole report is of great value.

Immunity. By JULIUS CITRON. Translated from the Second German Edition by A. L. GARBAT. $3.50. (*Philadelphia: P. Blakiston's Son & Co., 1914.*)

The popularity of this really excellent book is shown by the appearance of a second American edition within a year of the first translation. There are numerous additions and alterations which bring the work well up to date. These have been made in part by the editor, who has incorporated some of the more recent American work not covered in the German edition.

The book is not a text-book in the ordinary sense, but is designed as a compact and practical manual for the laboratory worker and for the clinician with some laboratory training. Detailed directions are given for carrying out, by the most approved methods, all the ordinary procedures of serum diagnosis. Special emphasis is placed on the possible sources of error and the control tests necessary to exclude them. The general principles and theories on which the tests are based also receive brief consideration.

The book will also be useful to the clinician in showing how these tests may be applied in practical diagnosis. Their limitations are pointed out and, as a rule, a commendable conservative attitude is maintained in discussing their reliability. The book contains an excellent chapter on tuberculin in diagnosis and treatment, as well as brief discussions of vaccine and serum therapy.

Progressive Medicine: A Quarterly Digest of Advances, Discoveries and Improvements in the Medical and Surgical Sciences. Edited by HOBART AMORY HARE, M. D., Philadelphia, assisted by LEIGHTON F. APPLEMAN, M. D., Philadelphia. Volume IV. December, 1914.

Diseases of the Digestive Tract and Allied Organs, the Liver, Pancreas and Peritoneum—Diseases of the Kidneys—Genito-Urinary Diseases—Surgery of the Extremities, Shock Anæsthesia, Infections, Fractures and Dislocations, and Tumors. Practical Therapeutic Referendum. (*Philadelphia and New York: Lea & Febiger, 1914.*)

In reading this quarterly digest of medical and surgical progress one is impressed by the immense range of literature covered by the various papers. Thus in surgery alone, including genito-urinary surgery, we find 175 out of a total of 405 pages; and yet hardly more than half a dozen topics have been touched upon. In elaborateness and thoroughness of treatment, although possibly not in literary form, many of the sections resemble the "Analytical and Critical Review," which filled such an important place in the English medical journals of a half century or more ago. It is interesting to observe that the newest literature is not only gathered together, but also carefully discussed and subjected to criticism. The need of such an assemblage and comparison of facts from widely different sources is well illustrated by Bloodgood's treatment of surgical shock in the volume before us. It is to be regretted that, like everyone else who has written upon the subject, he finds it easier to commend the methods adopted by surgeons to relieve shock than to explain its causation.

The section on therapeutics, under the rather pretentious title "Practical Therapeutic Referendum," is of equal value. It is not practicable to mention in detail the remaining sections of this excellent work. They are all real contributions to their respective branches of medicine and deserve a wide reading.

A Text-Book of Pathology for Students of Medicine. By J. GEORGE ADAMI, M. A., M. D., F. R. S., Strathcona Professor of Pathology, McGill University, and Advisory Pathologist to the Montreal General and the Royal Victoria Hospitals, Montreal, Canada; late Fellow of Jesus College, Cambridge, England; and JOHN MCCRAE, M. D., M. R. C. P. (Lond.), Lecturer in Pathology and Clinical Medicine, McGill University, Montreal; Senior Assistant Physician, Royal Victoria Hospital; Sometime Professor of Pathology, University of Vermont; late Fellow of Biology, University of Toronto, Toronto, Canada. Second edition, revised and enlarged. Illustrated with 395 engravings and 13 colored plates. (*Philadelphia and New York: Lea & Febiger, 1914.*)

We must agree with the authors "that the first edition of this text-book has measurably succeeded in its purpose is inferable from the early exhaustion of the large first edition." The second edition continues the same high standard which the authors reached in its predecessor. The orderly arrangement of the subject matter, the careful classification and correlation of the many facts, and their clear and concise presentation, particularly adapt the volume to its intended and entitled purpose. The aim of the authors to emphasize the reasons underlying pathological conditions is more than justified, since the ability to recognize individual pathological phenomena must, in great measure, be derived from actual experience. The changes in this edition are numerous. The syllabus at the head of each chapter is quite appropriate and most convenient. There is a new chapter on the more important infections. The chapter on monstrosities has been relegated to the appendix. There are a number of new illustrations. All these are decided improvements with the one possible exception, the change in nomenclature of tumors.

The book may be heartily recommended to students of pathology.

Practical Sanitation. A Handbook for Health Officers and Practitioners of Medicine. By FLETCHER GARDNER, M. D., and JAMES PERSONS SIMONDS, B. A., M. D. $4 net. (*St. Louis: C. V. Mosley Company, 1914.*)

This little publication by Gardner and Simonds contains a mass of information regarding sanitation, systematically arranged and of great value to health officers and physicians. The practical experience of the authors has shown the necessity of disseminating information of this character and "Practical Sanitation" deserves a wide circulation and a careful perusal by medical men.

ERRATUM.

February, 1915. The Recognition of Atypical Forms of Intestinal Amœbiasis. SELLARDS, A. W., and BAETJER, W. A.

Page 45, Outline, IV, 3, for *E. limax* read *limax.*

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